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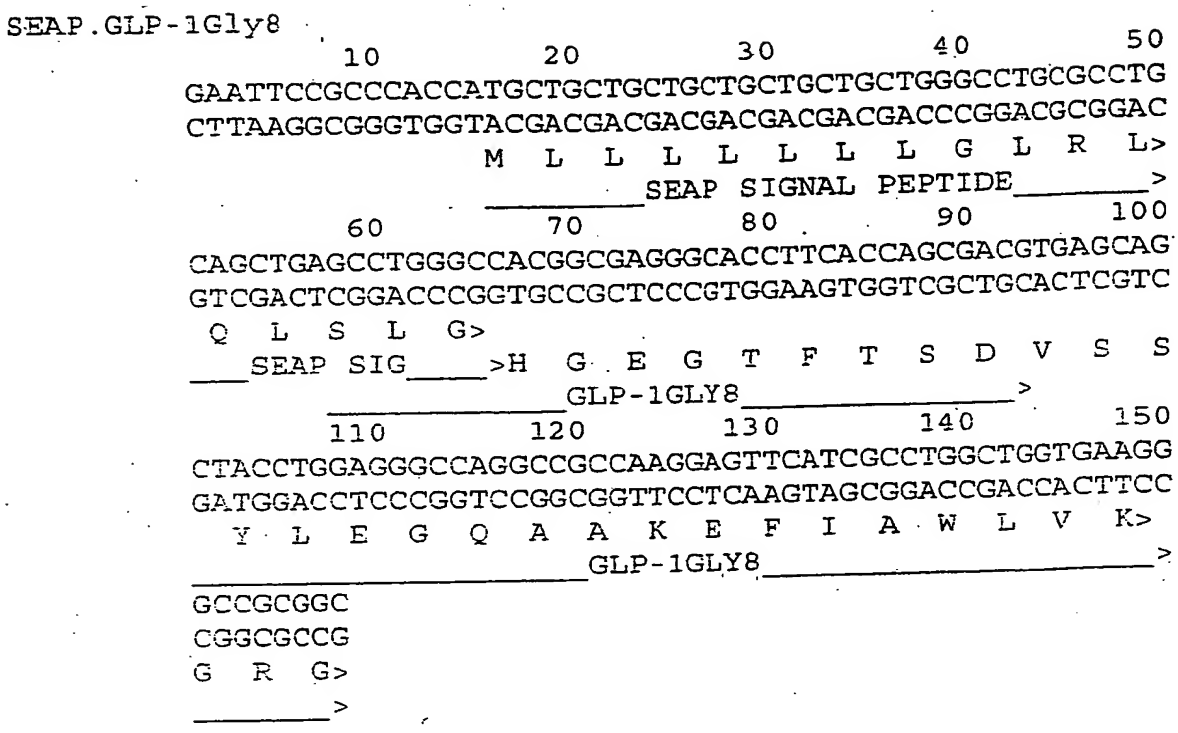

SEAP.GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGCTGCTGCTGCTGCTGCTGCTGGGCCTGCGCCTG
CTTAAGGCGGGTGGTACGACGACGACGACGACGACGACCCGGACGCGGAC
M L L L L L L L G L R L>
SEAP SIGNAL PEPTIDE
60 70 80 90 100
CAGCTGAGCCTGGGCCACGGCGAGGGCACCTTCACCAGCGACGTGAGCAG
GTCGACTCGGACCCGGTGCCGCTCCCGTGGAAGTGGTCGCTGCACTCGTC
Q L S L G>
SEAP SIG >H G E G T F T S D V S S
GLP-1GLY8
110 120 130 140 150
CTACCTGGAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAAGG
GATGGACCTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTTCC
Y L E G Q A A K E F I A W L V K>
GLP-1GLY8
GCCGCGGC
CGGCGCCG
G R G>
>

Figure 1

Exendin-4.GLP-1Gly8

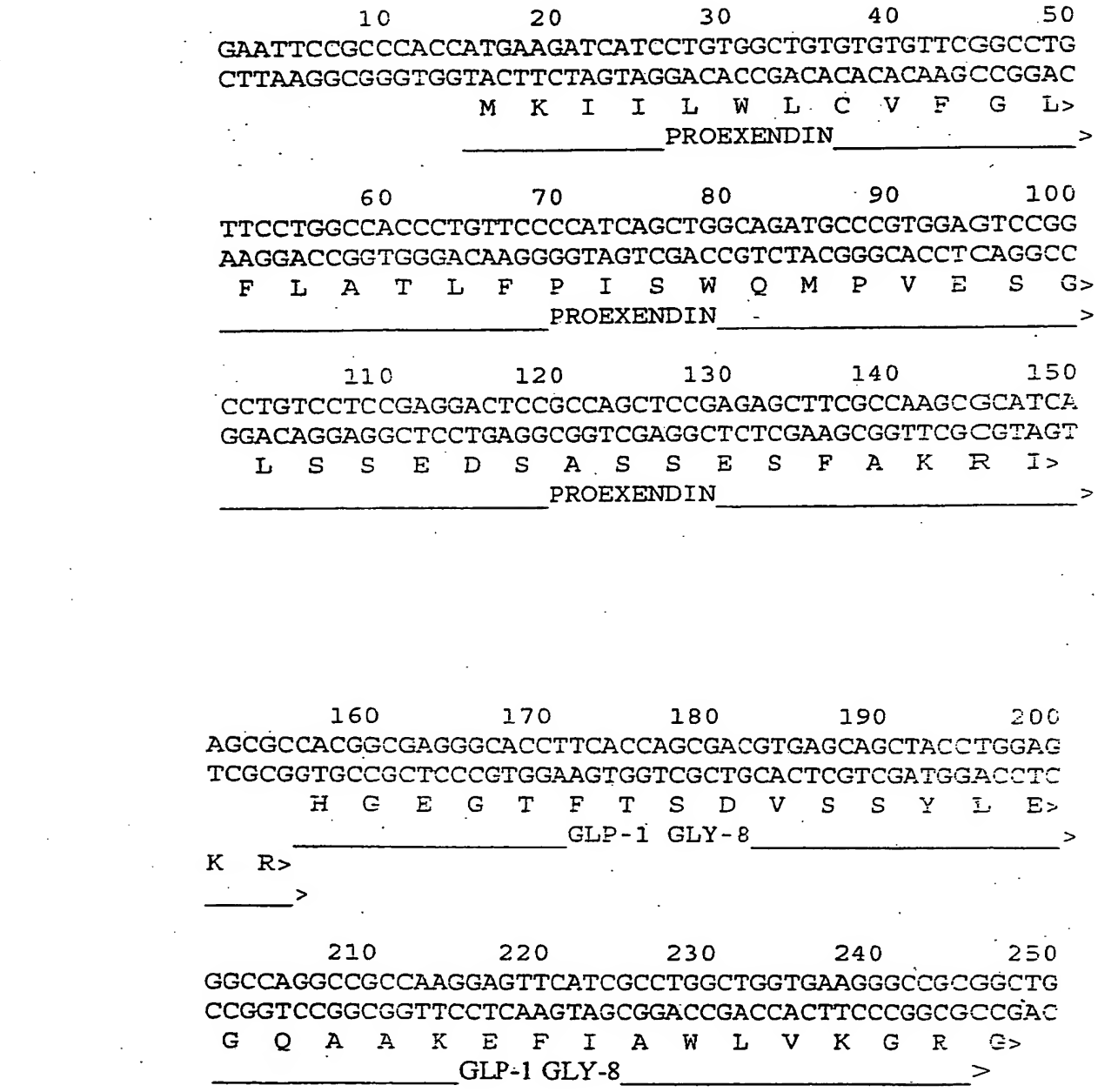


Figure 2

Helodermin.GLP-1Gly8

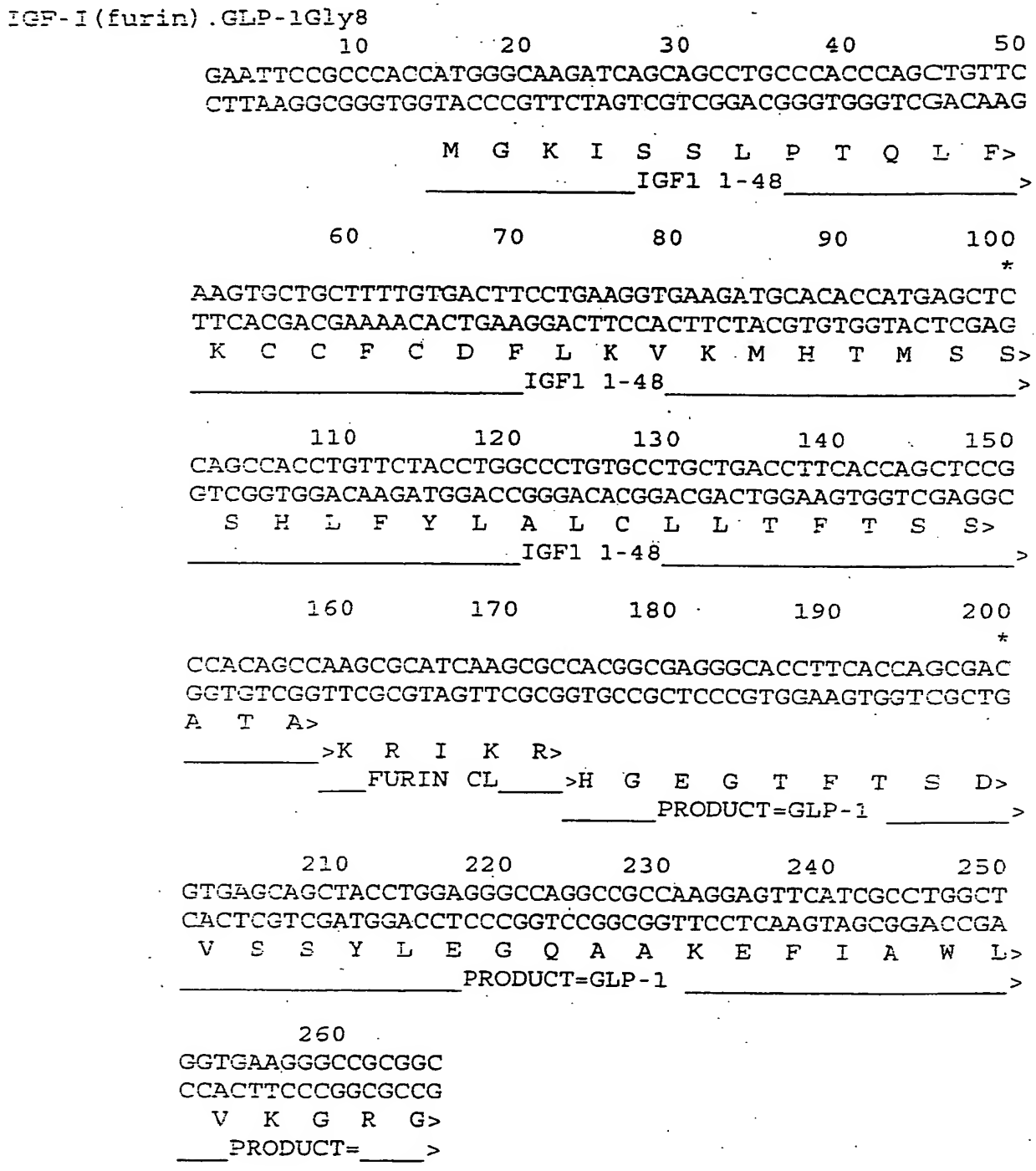
```
          10         20         30         40         50
GAATTCCGCCCACCATGAAGAGCATCCTGTGGCTGTGTGTGTTTGGCCTG
CTTAAGGCGGGTGGTACTTCTCGTAGGACACCGACACACACAAACCGGAC
                  M  K  S  I  L  W  L  C  V  F  G  L>
                 _____PRO-HELODERMIN_____>

          60         70         80         90        100
                                                      *
CTGATTGCCACCCTGTTCCCTGTGAGCTGGCAGATGGCCATCAAGAGCAG
GACTAACGGTGGGACAAGGGACACTCGACCGTCTACCGGTAGTTCTCGTC
 L  I  A  T  L  F  P  V  S  W  Q  M  A  I  K  S  R>
_____PRO-HELODERMIN_____>

         110        120        130        140        150
ACTGTCCTCTGAGGACTCTGAGACAGACCAGAGACTGAAGCGCATCAAGC
TGACAGGAGACTCCTGAGACTCTGTCTGGTCTCTGACTTCGCGTAGTTCG
  L  S  S  E  D  S  E  T  D  Q  R  L  K  R  I  K>
_____PRO-HELODERMIN_____>

         160        170        180        190        200
                                                      *
GCCACGGCGAGGGCACCTTCACCAGCGACGTGAGCAGCTACCTGGAGGGC
CGGTGCCGCTCCCGTGGAAGTGGTCGCTGCACTCGTCGATGGACCTCCCG
R>
   H  G  E  G  T  F  T  S  D  V  S  S  Y  L  E  G>
  _____PRODUCT=GLP-1 _____>

         210        220        230        240
CAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAAGGGCCGCGGC
GTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTTCCCGGCGCCG

 Q  A  A  K  E  F  I  A  W  L  V  K  G  R  G>
_____PRODUCT=GLP-1 _____>
```

Figure 3

GIP.GLP-1Gly8

```
          10         20         30         40         50
GAATTCCGCCCACCATGGTGGCCACCAAGACCTTTGCCCTGCTGCTCCTG
CTTAAGGCGGGTGGTACCACCGGTGGTTCTGGAAACGGGACGACGAGGAC
                M  V  A  T  K  T  F  A  L  L  L  L>
                _____________PRO-GIP_____________>

          60         70         80         90        100
                                                      *
AGCCTCTTCCTGGCTGTGGGACTGGGCGAGAAGAAGGAAGGCCACTTCAG
TCGGAGAAGGACCGACACCCTGACCCGCTCTTCTTCCTTCCGGTGAAGTC
 S  L  F  L  A  V  G  L  G  E  K  K  E  G  H  F  S>
_________________________PRO-GIP_________________________>

         110        120        130        140        150
CGCCCTGCCCAGCCTGCCAGTGGGCAGCCATGCCAAGGTGAGCTCCCCAC
GCGGGACGGGTCGGACGGTCACCCGTCGGTACGGTTCCACTCGAGGGGTG
  A  L  P  S  L  P  V  G  S  H  A  K  V  S  S  P>
_________________________PRO-GIP_________________________>

         160        170        180        190        200
                                                      *
AGAAGCGCATCAAGCGCCACGGCGAGGGCACCTTCACCAGCGACGTGAGC
TCTTCGCGTAGTTCGCGGTGCCGCTCCCGTGGAAGTGGTCGCTGCACTCG
Q  K  R  I  K  R>
_____PRO-GIP_____>H  G  E  G  T  F  T  S  D  V  S>
                  ___________GLP-1GLY8___________>

         210        220        230        240        250
AGCTACCTGGAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAA
TCGATGGACCTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTT
 S  Y  L  E  G  Q  A  A  K  E  F  I  A  W  L  V  K>
_________________________GLP-1GLY8_________________________>

         260
GGGCCGCGGC
CCCGGCGCCG
  G  R  G>
_________>
```

Figure 4


IGF-I(furin).GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGGGCAAGATCAGCAGCCTGCCCACCCAGCTGTTC
CTTAAGGCGGGTGGTACCCGTTCTAGTCGTCGGACGGGTGGGTCGACAAG
M G K I S S L P T Q L F>
IGF1 1-48>
60 70 80 90 100
AAGTGCTGCTTTTGTGACTTCCTGAAGGTGAAGATGCACACCATGAGCTC
TTCACGACGAAAACACTGAAGGACTTCCACTTCTACGTGTGGTACTCGAG
K C C F C D F L K V K M H T M S S>
IGF1 1-48>
110 120 130 140 150
CAGCCACCTGTTCTACCTGGCCCTGTGCCTGCTGACCTTCACCAGCTCCG
GTCGGTGGACAAGATGGACCGGGACACGGACGACTGGAAGTGGTCGAGGC
S H L F Y L A L C L L T F T S S>
IGF1 1-48>
160 170 180 190 200
CCACAGCCAAGCGCATCAAGCGCCACGGCGAGGGCACCTTCACCAGCGAC
GGTGTCGGTTCGCGTAGTTCGCGGTGCCGCTCCCGTGGAAGTGGTCGCTG
A T A>
>K R I K R>
FURIN CL>H G E G T F T S D>
PRODUCT=GLP-1 >
210 220 230 240 250
GTGAGCAGCTACCTGGAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGCT
CACTCGTCGATGGACCTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCGA
V S S Y L E G Q A A K E F I A W L>
PRODUCT=GLP-1 >
260
GGTGAAGGGCCGCGGC
CCACTTCCCGGCGCCG
V K G R G>
PRODUCT=>
Figure 5

IGF-I.GLP-1Gly8

```
                10        20        30        40        50
GAATTCCGCCCACCATGGGCAAGATCAGCAGCCTGCCCACCCAGCTGTTC
CTTAAGGCGGGTGGTACCCGTTCTAGTCGTCGGACGGGTGGGTCGACAAG
                  M  G  K  I  S  S  L  P  T  Q  L  F>
                 _____IGF-I SIGNAL PEPTIDE_____>

        60        70        80        90       100
                                                   *
AAGTGCTGCTTTTGTGACTTCCTGAAGGTGAAGATGCACACCATGAGCTC

TTCACGACGAAAACACTGAAGGACTTCCACTTCTACGTGTGGTACTCGAG
 K  C  C  F  C  D  F  L  K  V  K  M  H  T  M  S  S>
_____IGF-I SIGNAL PEPTIDE_____>

       110       120       130       140       150
CAGCCACCTGTTCTACCTGGCCCTGTGCCTGCTGACCTTCACCAGCTCCG
GTCGGTGGACAAGATGGACCGGGACACGGACGACTGGAAGTGGTCGAGGC
  S  H  L  F  Y  L  A  L  C  L  L  T  F  T  S  S>
_____IGF-I SIGNAL PEPTIDE_____>

       160       170       180       190       200
                                                   *
CCACAGCCCACGGCGAGGGCACCTTCACCAGCGACGTGAGCAGCTACCTG
GGTGTCGGGTGCCGCTCCCGTGGAAGTGGTCGCTGCACTCGTCGATGGAC
A  T  A>
_____>H  G  E  G  T  F  T  S  D  V  S  S  Y  L>
      _____GLP-1GLY8_____>

       210       220       230       240       250
GAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAAGGGCCGCGGC
CTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTTCCCGGCGCCG
 E  G  Q  A  A  K  E  F  I  A  W  L  V  K  G  R  G>
_____GLP-1GLY8_____>
```

Figure 6

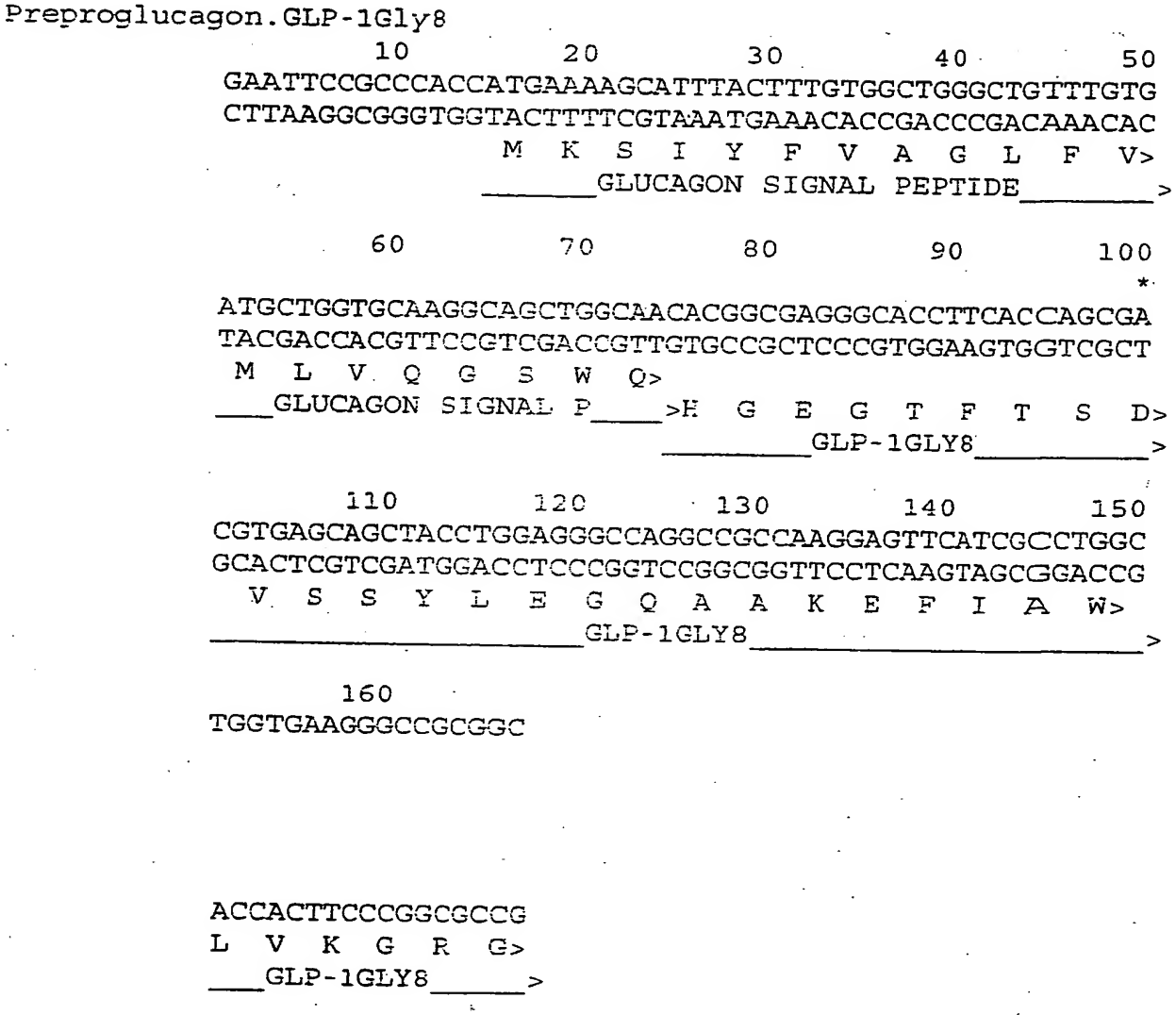

Preproglucagon.GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGAAAAGCATTTACTTTGTGGCTGGGCTGTTTGTG
CTTAAGGCGGGTGGTACTTTTCGTAAATGAAACACCGACCCGACAAACAC
M K S I Y F V A G L F V>
GLUCAGON SIGNAL PEPTIDE
60 70 80 90 100
ATGCTGGTGCAAGGCAGCTGGCAACACGGCGAGGGCACCTTCACCAGCGA
TACGACCACGTTCCGTCGACCGTTGTGCCGCTCCCGTGGAAGTGGTCGCT
M L V Q G S W Q>
GLUCAGON SIGNAL P >H G E G T F T S D>
GLP-1GLY8
110 120 130 140 150
CGTGAGCAGCTACCTGGAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGC
GCACTCGTCGATGGACCTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCG
V S S Y L E G Q A A K E F I A W>
GLP-1GLY8
160
TGGTGAAGGGCCGCGGC
ACCACTTCCCGGCGCCG
L V K G R G>
GLP-1GLY8

Figure 7

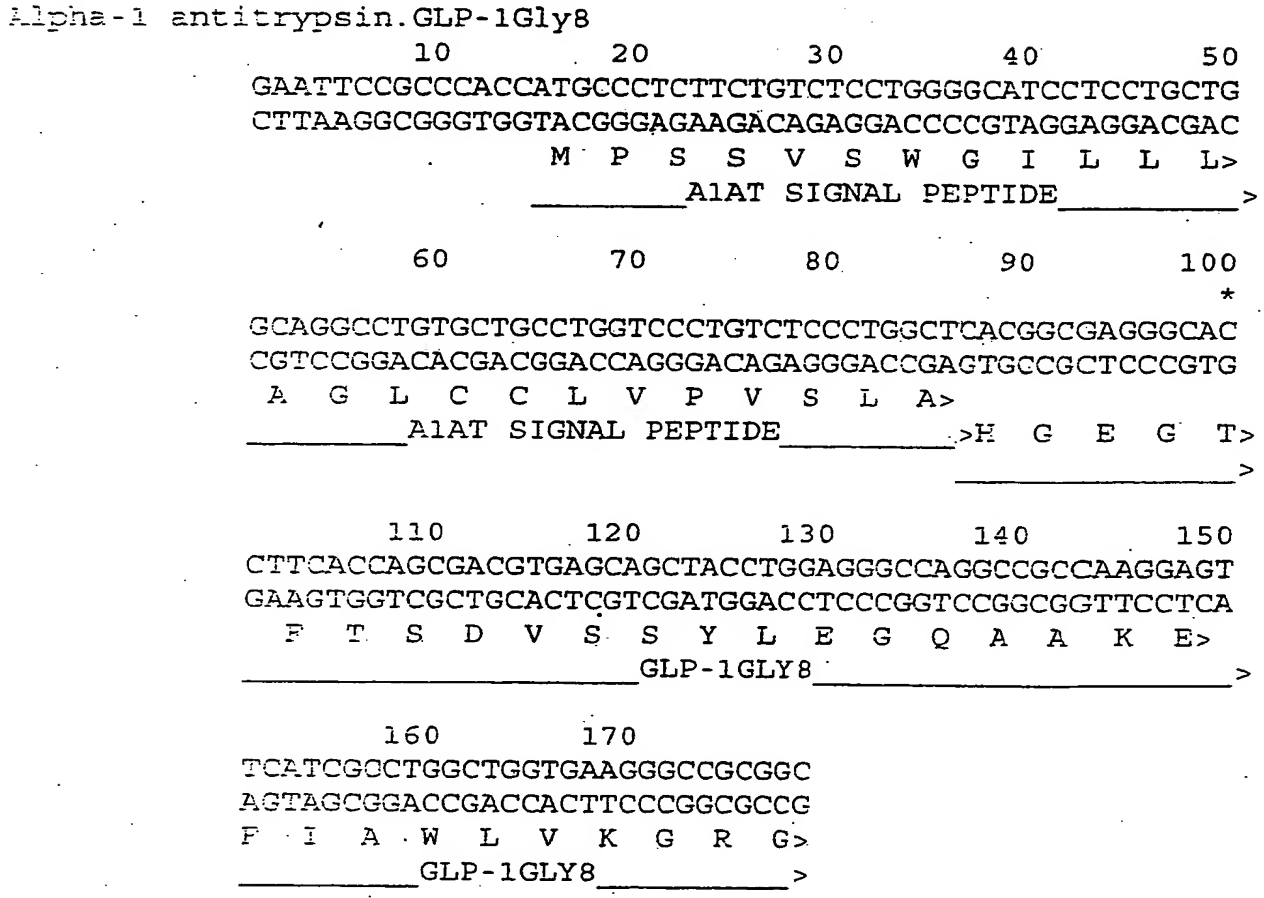

Alpha-1 antitrypsin.GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGCCCTCTTCTGTCTCCTGGGGCATCCTCCTGCTG
CTTAAGGCGGGTGGTACGGGAGAAGACAGAGGACCCCGTAGGAGGACGAC
M P S S V S W G I L L L>
A1AT SIGNAL PEPTIDE
60 70 80 90 100
GCAGGCCTGTGCTGCCTGGTCCCTGTCTCCCTGGCTCACGGCGAGGGCAC
CGTCCGGACACGACGGACCAGGGACAGAGGGACCGAGTGCCGCTCCCGTG
A G L C C L V P V S L A>
A1AT SIGNAL PEPTIDE>H G E G T>
110 120 130 140 150
CTTCACCAGCGACGTGAGCAGCTACCTGGAGGGCCAGGCCGCCAAGGAGT
GAAGTGGTCGCTGCACTCGTCGATGGACCTCCCGGTCCGGCGGTTCCTCA
F T S D V S S Y L E G Q A A K E>
GLP-1GLY8
160 170
TCATCGCCTGGCTGGTGAAGGGCCGCGGC
AGTAGCGGACCGACCACTTCCCGGCGCCG
F I A W L V K G R G>
GLP-1GLY8>

Figure 8

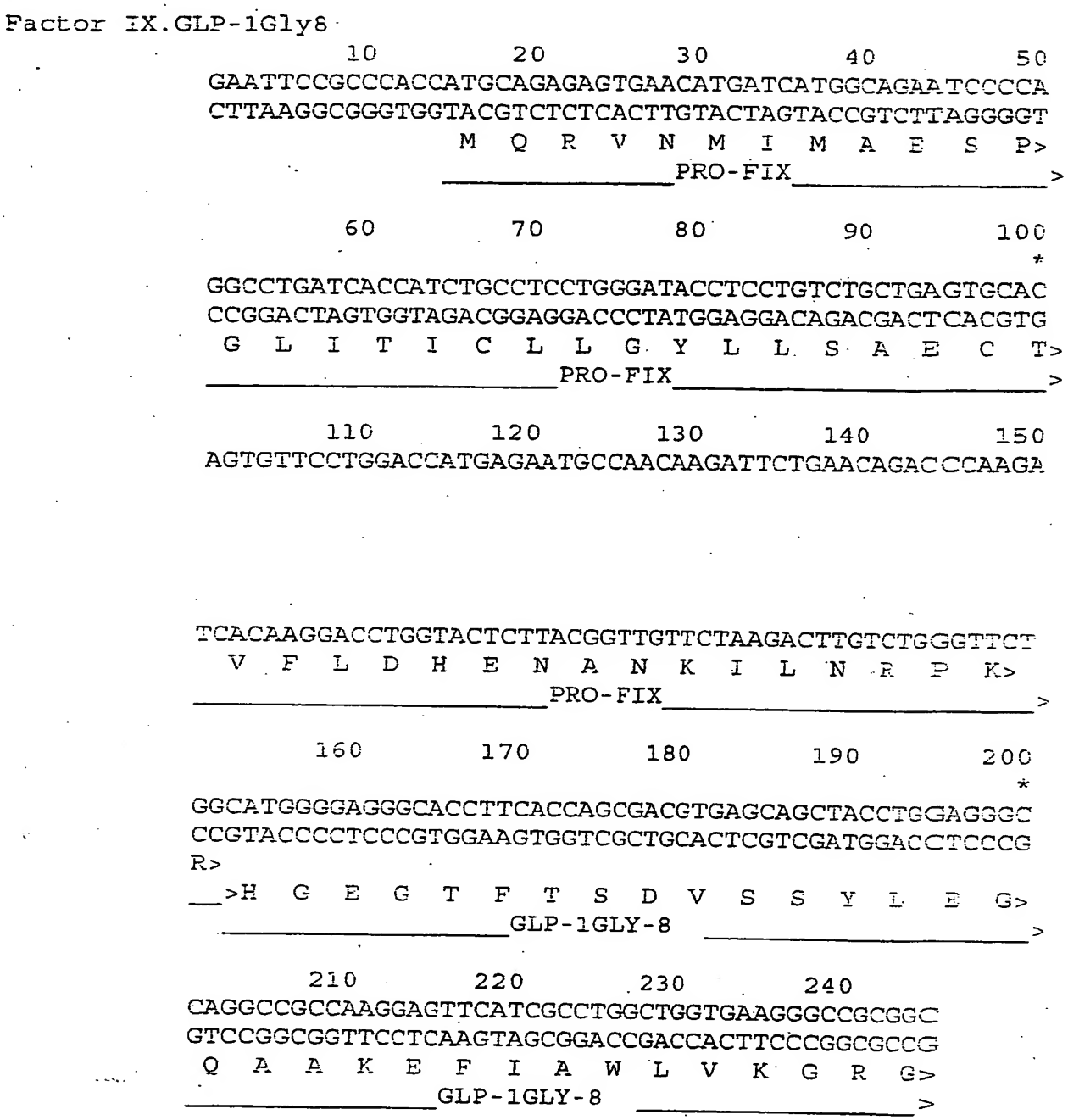

Factor IX.GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGCAGAGAGTGAACATGATCATGGCAGAATCCCCA
CTTAAGGCGGGTGGTACGTCTCTCACTTGTACTAGTACCGTCTTAGGGGT
M Q R V N M I M A E S P>
PRO-FIX>
60 70 80 90 100
GGCCTGATCACCATCTGCCTCCTGGGATACCTCCTGTCTGCTGAGTGCAC
CCGGACTAGTGGTAGACGGAGGACCCTATGGAGGACAGACGACTCACGTG
G L I T I C L L G Y L L S A E C T>
PRO-FIX>
110 120 130 140 150
AGTGTTCCTGGACCATGAGAATGCCAACAAGATTCTGAACAGACCCAAGA
TCACAAGGACCTGGTACTCTTACGGTTGTTCTAAGACTTGTCTGGGTTCT
V F L D H E N A N K I L N R P K>
PRO-FIX>
160 170 180 190 200
GGCATGGGGAGGGCACCTTCACCAGCGACGTGAGCAGCTACCTGGAGGGC
CCGTACCCCTCCCGTGGAAGTGGTCGCTGCACTCGTCGATGGACCTCCCG
R>
>H G E G T F T S D V S S Y L E G>
GLP-1GLY-8
210 220 230 240
CAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAAGGGCCGCGGC
GTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTTCCCGGCGCCG
Q A A K E F I A W L V K G R G>
GLP-1GLY-8

Figure 9

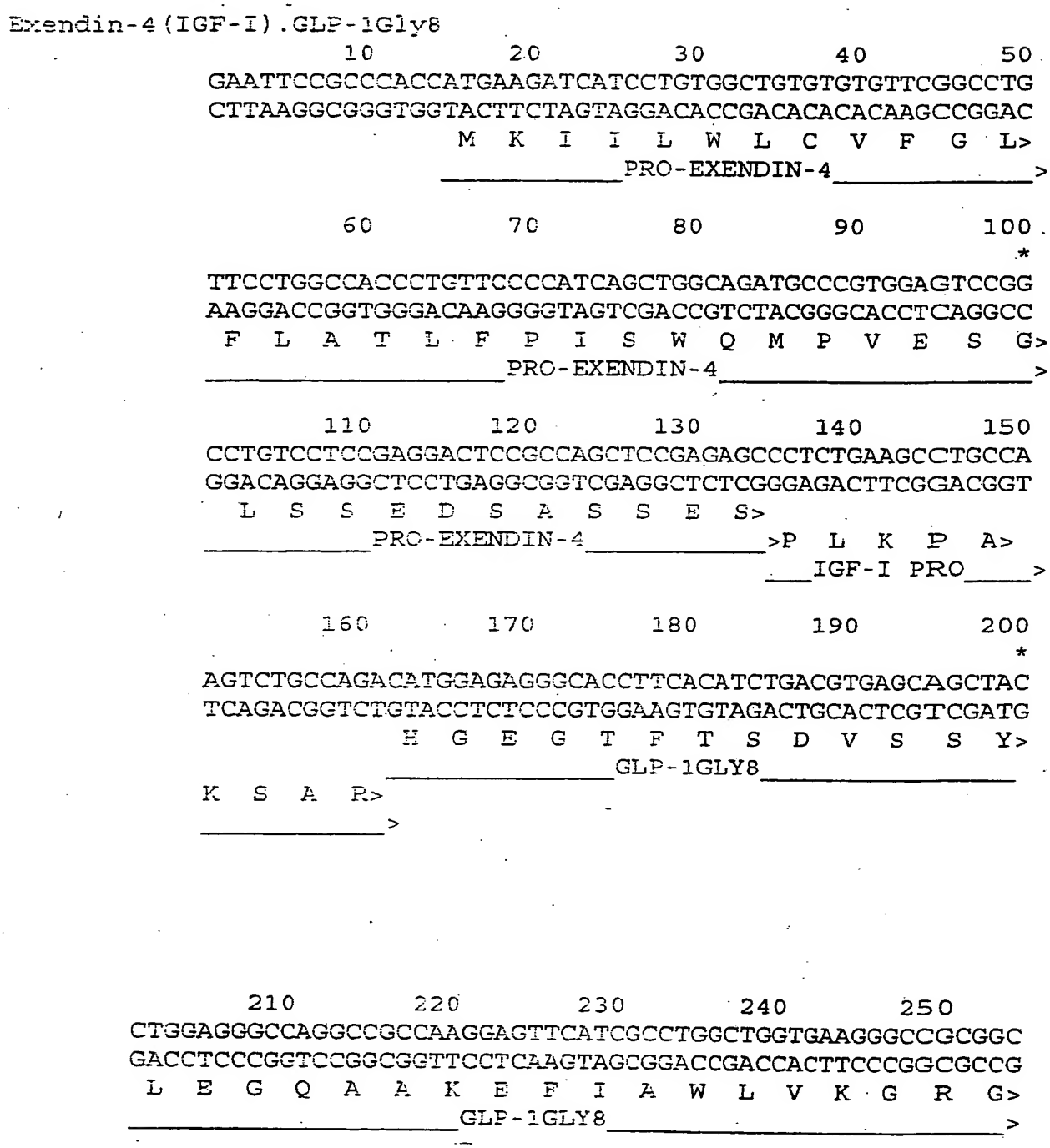

Exendin-4(IGF-I).GLP-1Gly8
10 20 30 40 50
GAATTCCGCCCACCATGAAGATCATCCTGTGGCTGTGTGTGTTCGGCCTG
CTTAAGGCGGGTGGTACTTCTAGTAGGACACCGACACACACAAGCCGGAC
M K I I L W L C V F G L>
PRO-EXENDIN-4
60 70 80 90 100
TTCCTGGCCACCCTGTTCCCCATCAGCTGGCAGATGCCCGTGGAGTCCGG
AAGGACCGGTGGGACAAGGGGTAGTCGACCGTCTACGGGCACCTCAGGCC
F L A T L F P I S W Q M P V E S G>
PRO-EXENDIN-4
110 120 130 140 150
CCTGTCCTCCGAGGACTCCGCCAGCTCCGAGAGCCCTCTGAAGCCTGCCA
GGACAGGAGGCTCCTGAGGCGGTCGAGGCTCTCGGGAGACTTCGGACGGT
L S S E D S A S S E S>
PRO-EXENDIN-4
>P L K P A>
IGF-I PRO
160 170 180 190 200
AGTCTGCCAGACATGGAGAGGGCACCTTCACATCTGACGTGAGCAGCTAC
TCAGACGGTCTGTACCTCTCCCGTGGAAGTGTAGACTGCACTCGTCGATG
H G E G T F T S D V S S Y>
GLP-1GLY8
K S A R>
210 220 230 240 250
CTGGAGGGCCAGGCCGCCAAGGAGTTCATCGCCTGGCTGGTGAAGGGCCGCGGC
GACCTCCCGGTCCGGCGGTTCCTCAAGTAGCGGACCGACCACTTCCCGGCGCCG
L E G Q A A K E F I A W L V K G R G>
GLP-1GLY8

Figure 10

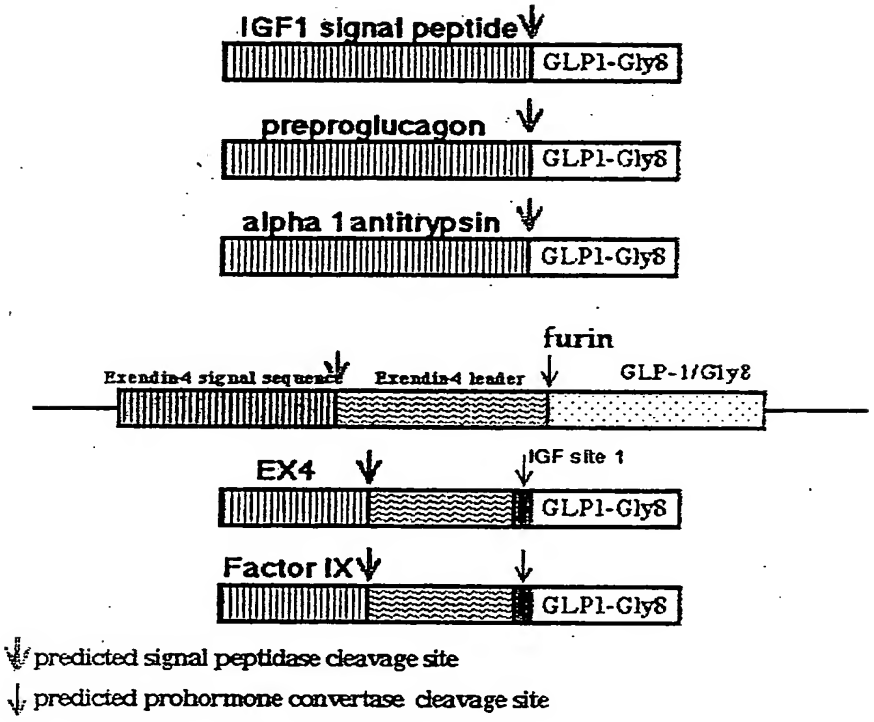

IGF1 signal peptide
GLP1-Gly8
preproglucagon
GLP1-Gly8
alpha 1antitrypsin
GLP1-Gly8
furin
Exendin-4 signal sequence
Exendin-4 leader
GLP-1/Gly8
EX4
IGF site 1
GLP1-Gly8
Factor IX
GLP1-Gly8
predicted signal peptidase cleavage site
predicted prohormone convertase cleavage site

Figure 11

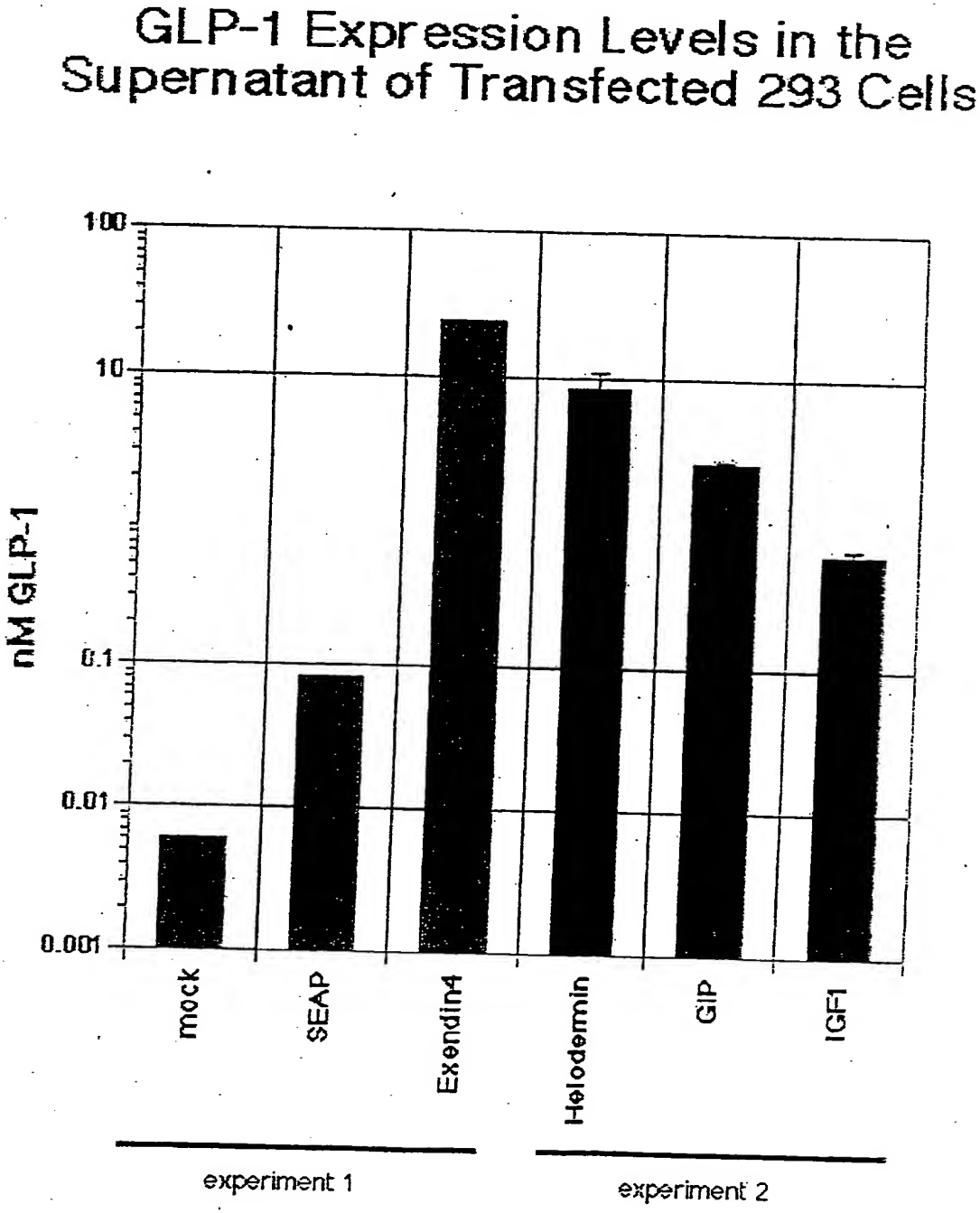

GLP-1 Expression Levels in the Supernatant of Transfected 293 Cells
nM GLP-1
100
10
0.1
0.01
0.001
mock
SEAP
Exendin4
Helodermin
GIP
IGF1
experiment 1
experiment 2

Figure 12

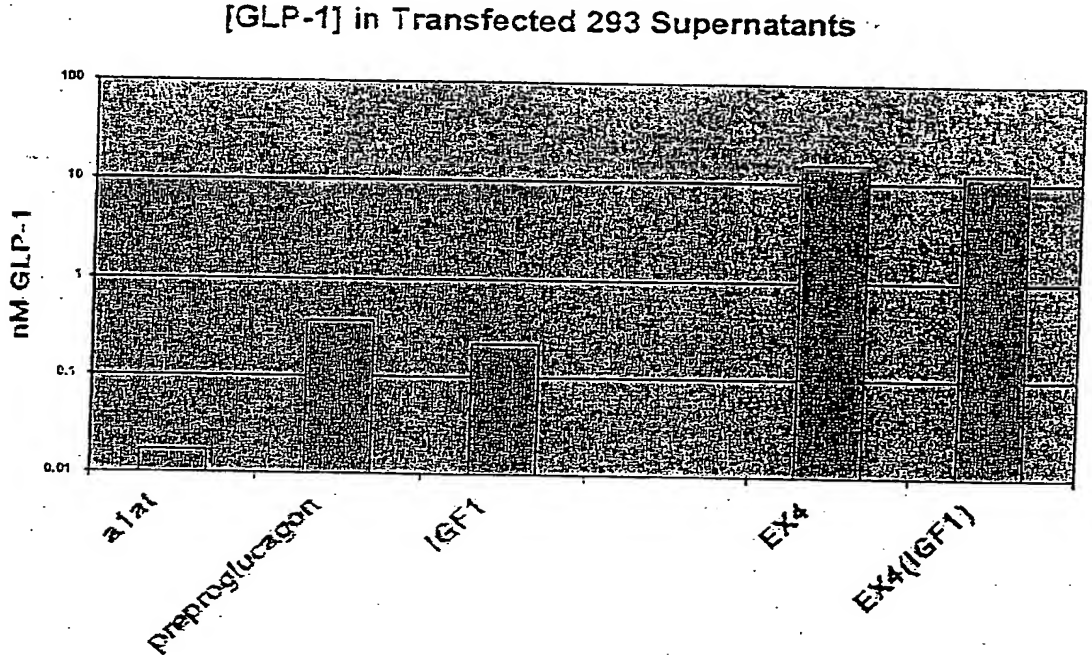

[GLP-1] in Transfected 293 Supernatants
nM GLP-1
100
10
1
0.1
0.01
alat
Preproglucagon
IGF1
EX4
EX4(IGF1)

Figure 13

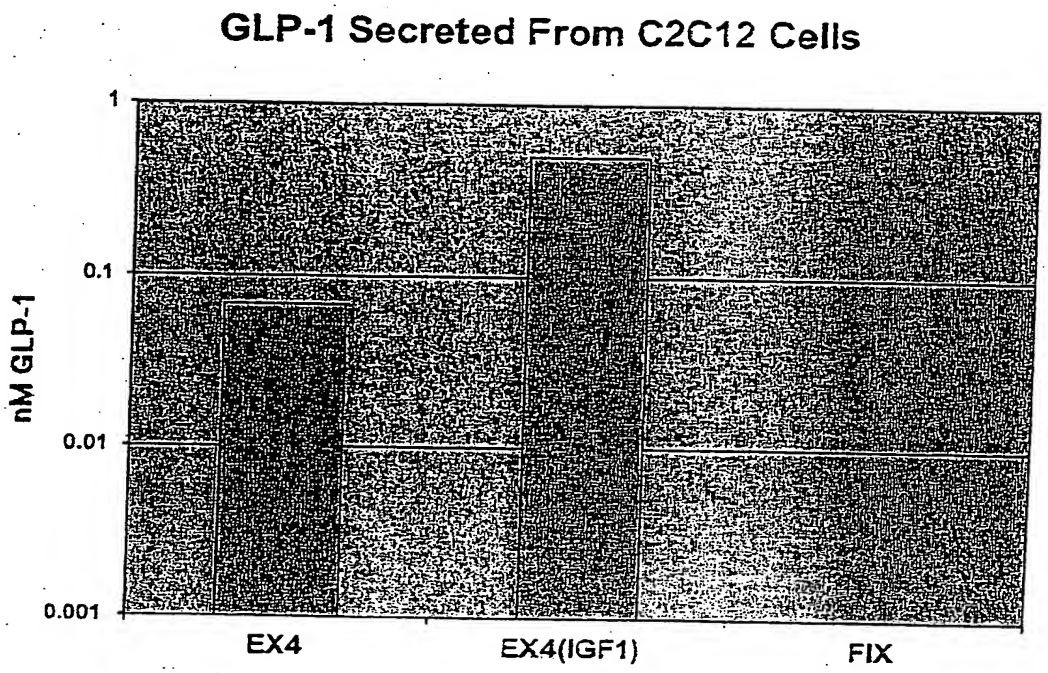

GLP-1 Secreted From C2C12 Cells
nM GLP-1
1
0.1
0.01
0.001
EX4
EX4(IGF1)
FIX

Figure 14

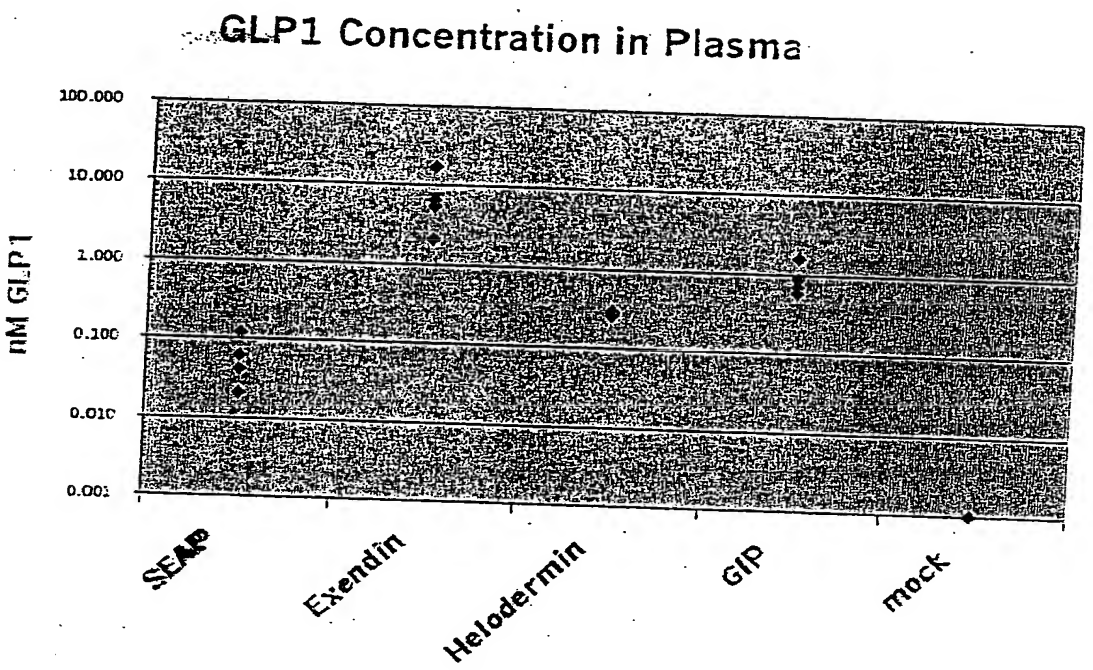

GLP1 Concentration in Plasma
100.000
10.000
1.000
0.100
0.010
0.001
nM GLP1
SEAP
Exendin
Helodermin
GIP
mock

Figure 15

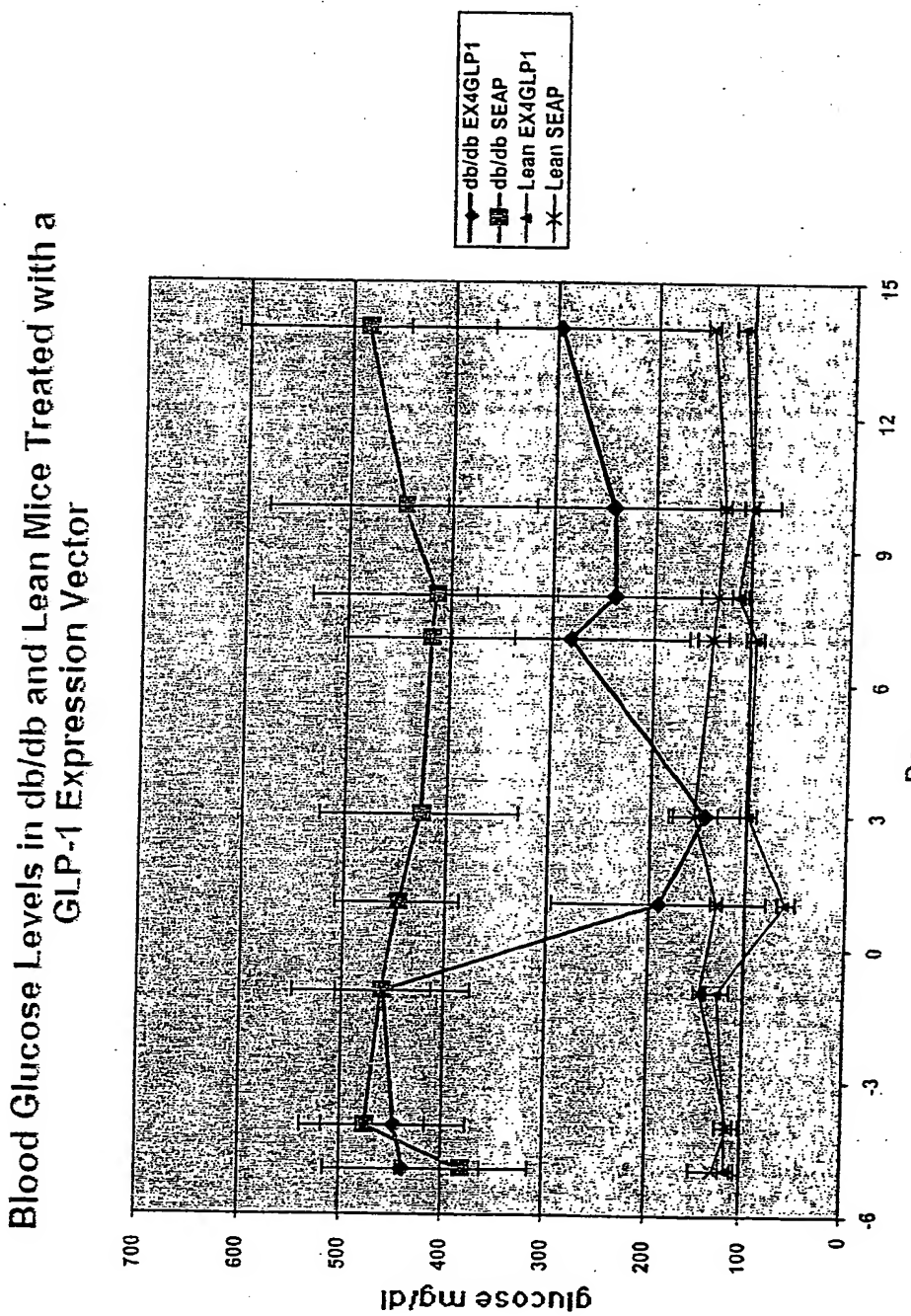

Blood Glucose Levels in db/db and Lean Mice Treated with a GLP-1 Expression Vector
db/db EX4GLP1
db/db SEAP
Lean EX4GLP1
Lean SEAP
glucose mg/dl
0
100
200
300
400
500
600
700
Day
-6
-3
0
3
6
9
12
15

Figure 16

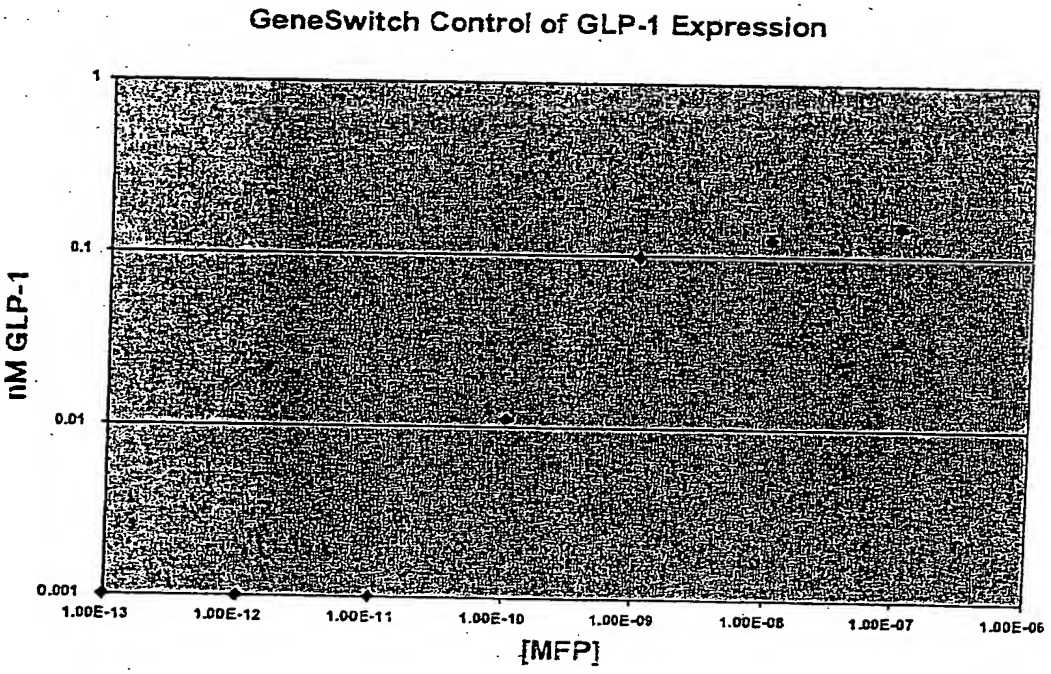

GeneSwitch Control of GLP-1 Expression
1
0.1
0.01
0.001
nM GLP-1
1.00E-13
1.00E-12
1.00E-11
1.00E-10
1.00E-09
1.00E-08
1.00E-07
1.00E-06
[MFP]

Figure 17

Examples of Modified GLP-1

His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys (SEQ ID NO:23)

His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35} (SEQ ID NO: 24)

His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg (SEQ ID NO:25)

His^{7}-Val-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:26)

His^{7}-Ala-Gln-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:27)

His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Thr-Ser-Lys-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37} (SEQ ID NO:28)

His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Lys-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:29)

^{His7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-D-GLn^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:30)

Figure 18A

Asp-Glu-Phe-Glu-Arg-His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:31)

Glu-Phe-Glu-Arg-His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:32)

Arg-His^{7}-Ala-Glu-Gly^{10}-Thr-Phe-Thr-Ser-Asp^{15}-Val-Ser-Ser-Tyr-Leu^{20}-Glu-Gly-Gln-Ala-Ala^{25}-Lys-Glu-Phe-Ile-Ala^{30}-Trp-Leu-Val-Lys-Gly^{35}-Arg-Gly^{37}-COOH (SEQ ID NO:33)

Figure 18B

Figure 19

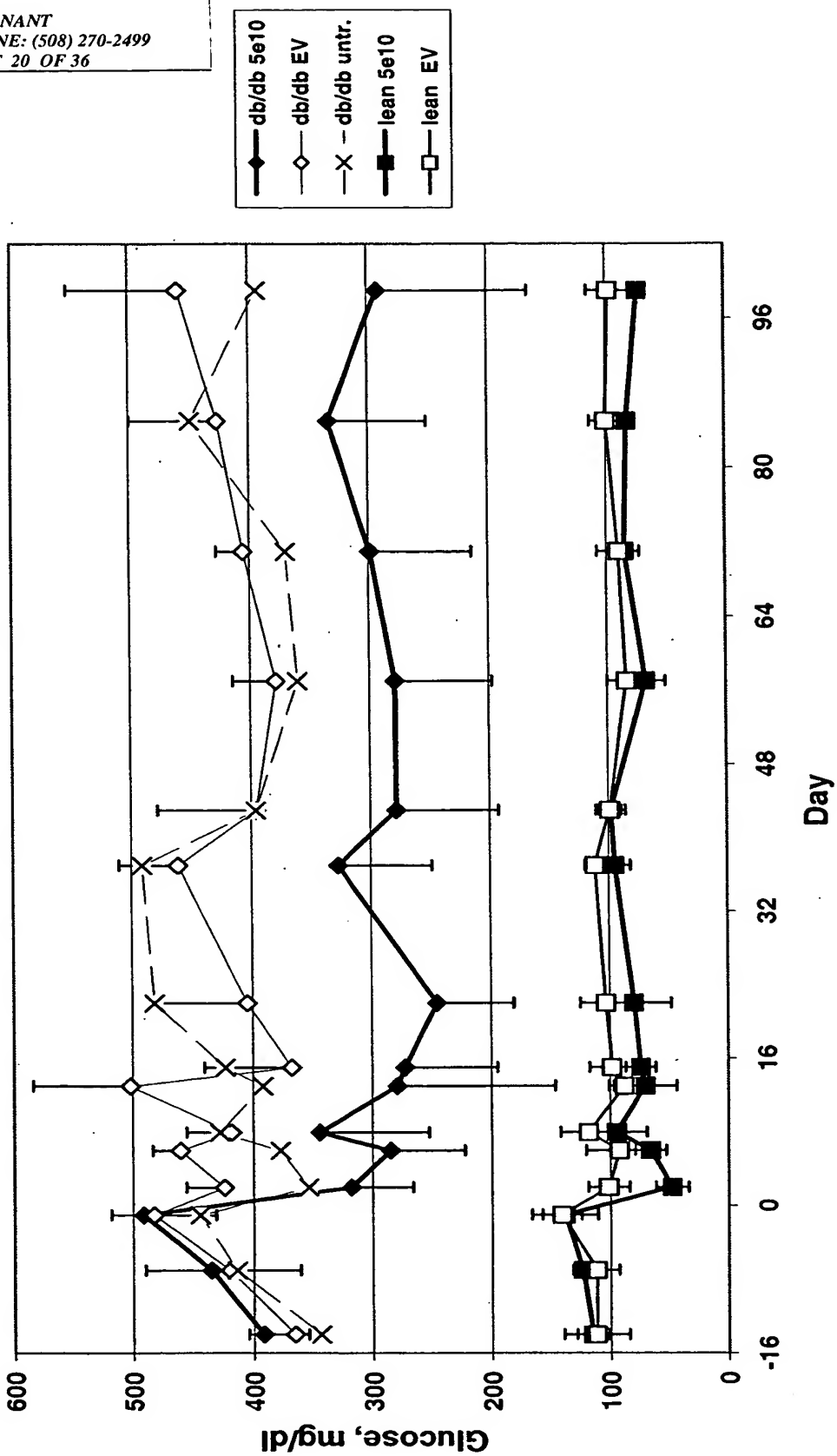

db/db 5e10
db/db EV
db/db untr.
lean 5e10
lean EV
Glucose, mg/dl
600
500
400
300
200
100
0
Day
-16
0
16
32
48
64
80
96

Figure 20

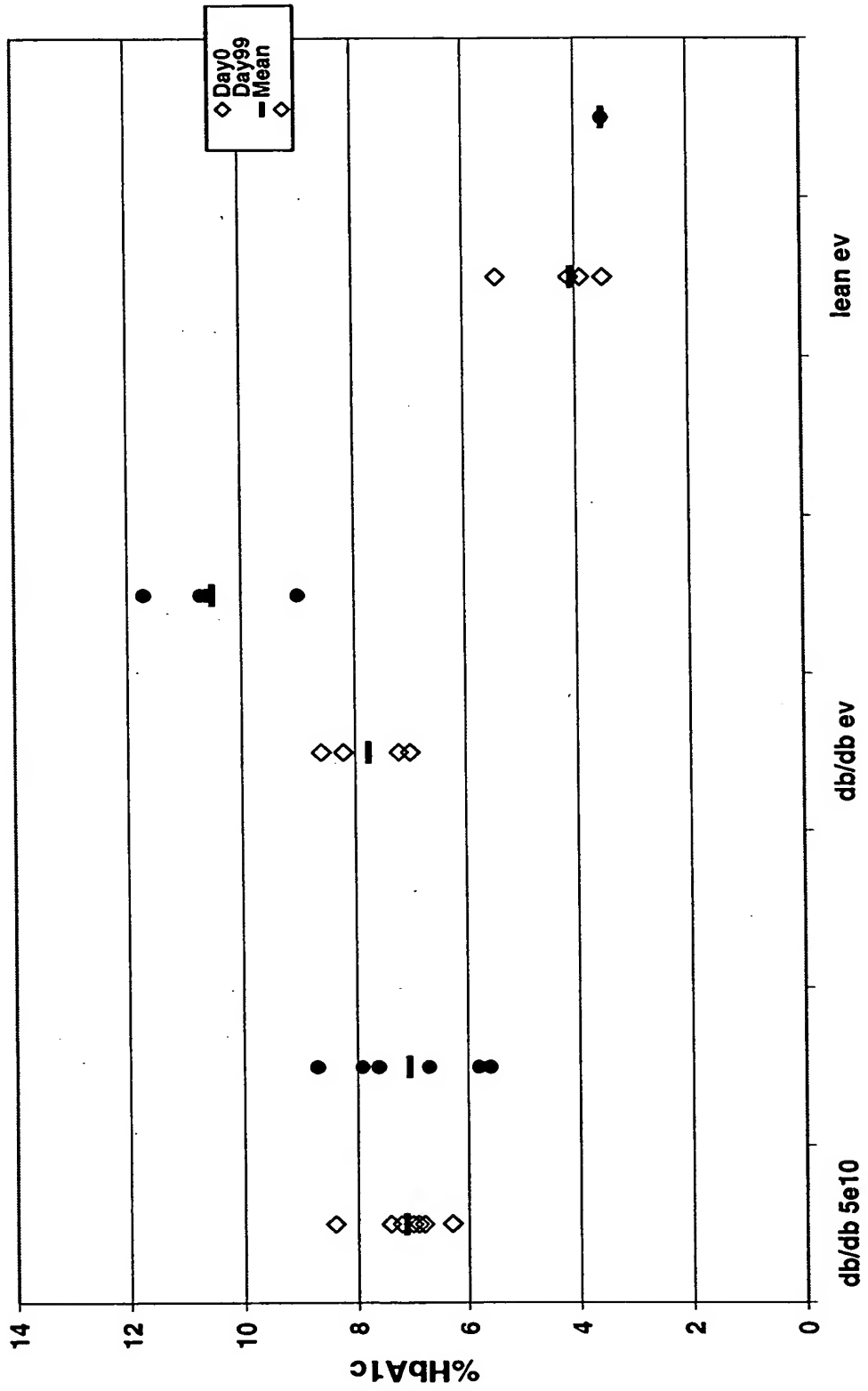


Figure 21

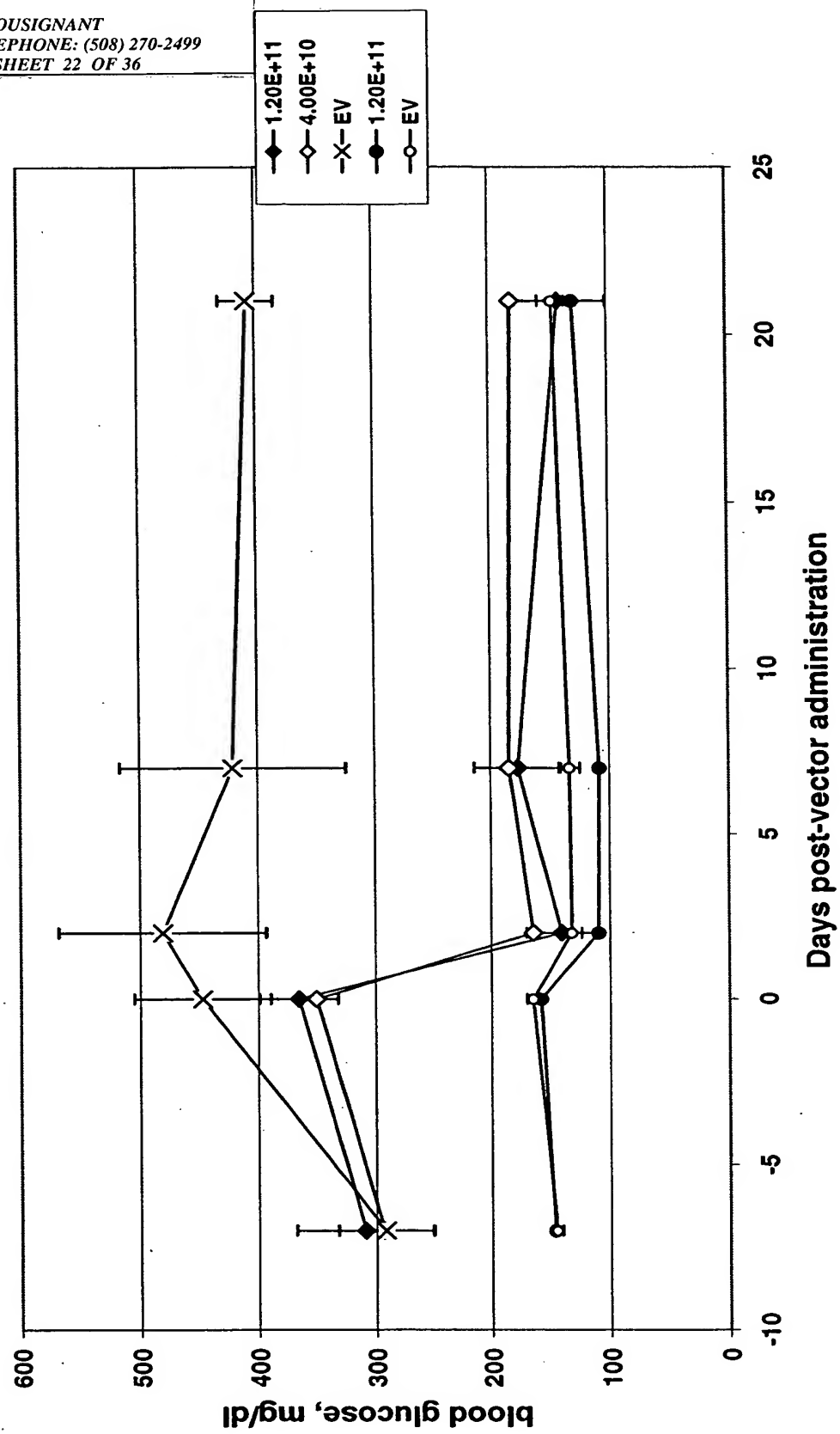

1.20E+11
4.00E+10
EV
1.20E+11
EV
blood glucose, mg/dl
600
500
400
300
200
100
0
Days post-vector administration
25
20
15
10
5
0
-5
-10

Figure 22

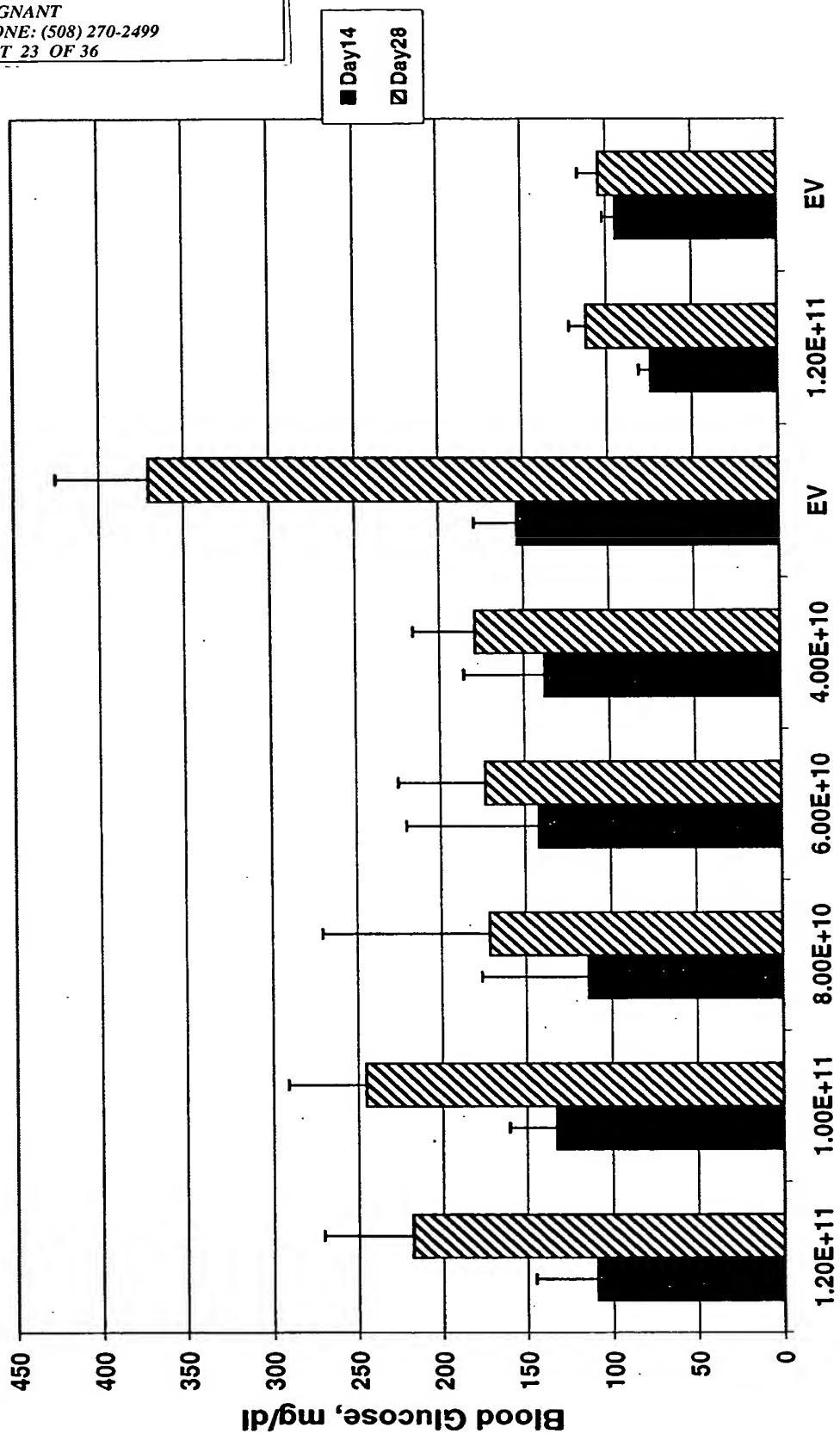

Day14
Day28
Blood Glucose, mg/dl
0
50
100
150
200
250
300
350
400
450
EV
1.20E+11
EV
4.00E+10
6.00E+10
8.00E+10
1.00E+11
1.20E+11

Figure 23

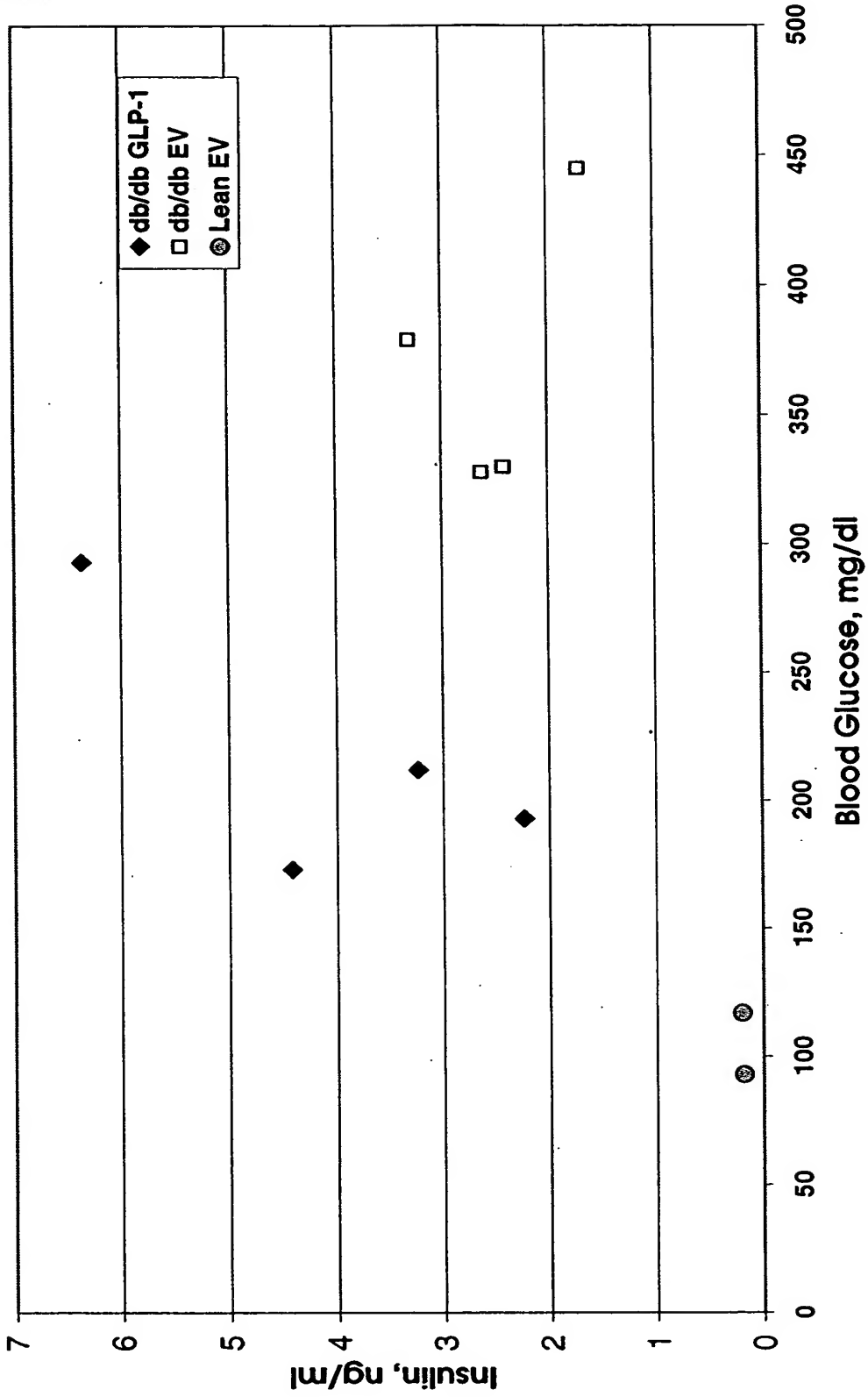

db/db GLP-1
db/db EV
Lean EV
Insulin, ng/ml
0
1
2
3
4
5
6
7
Blood Glucose, mg/dl
0
50
100
150
200
250
300
350
400
450
500

Figure 24

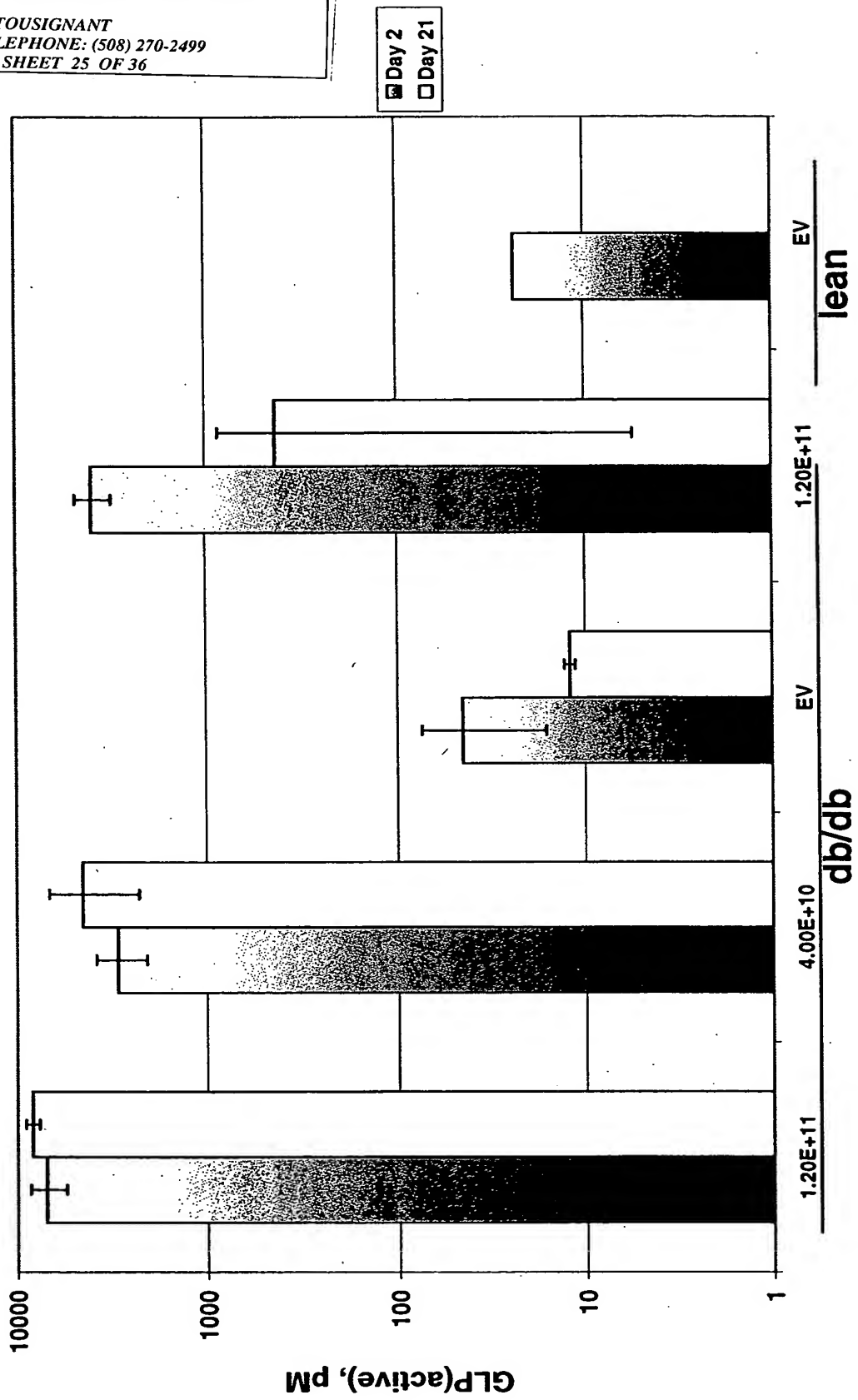

Day 2
Day 21
GLP(active), pM
10000
1000
100
10
1
EV
1.20E+11
EV
4.00E+10
1.20E+11
lean
db/db

Figure 25

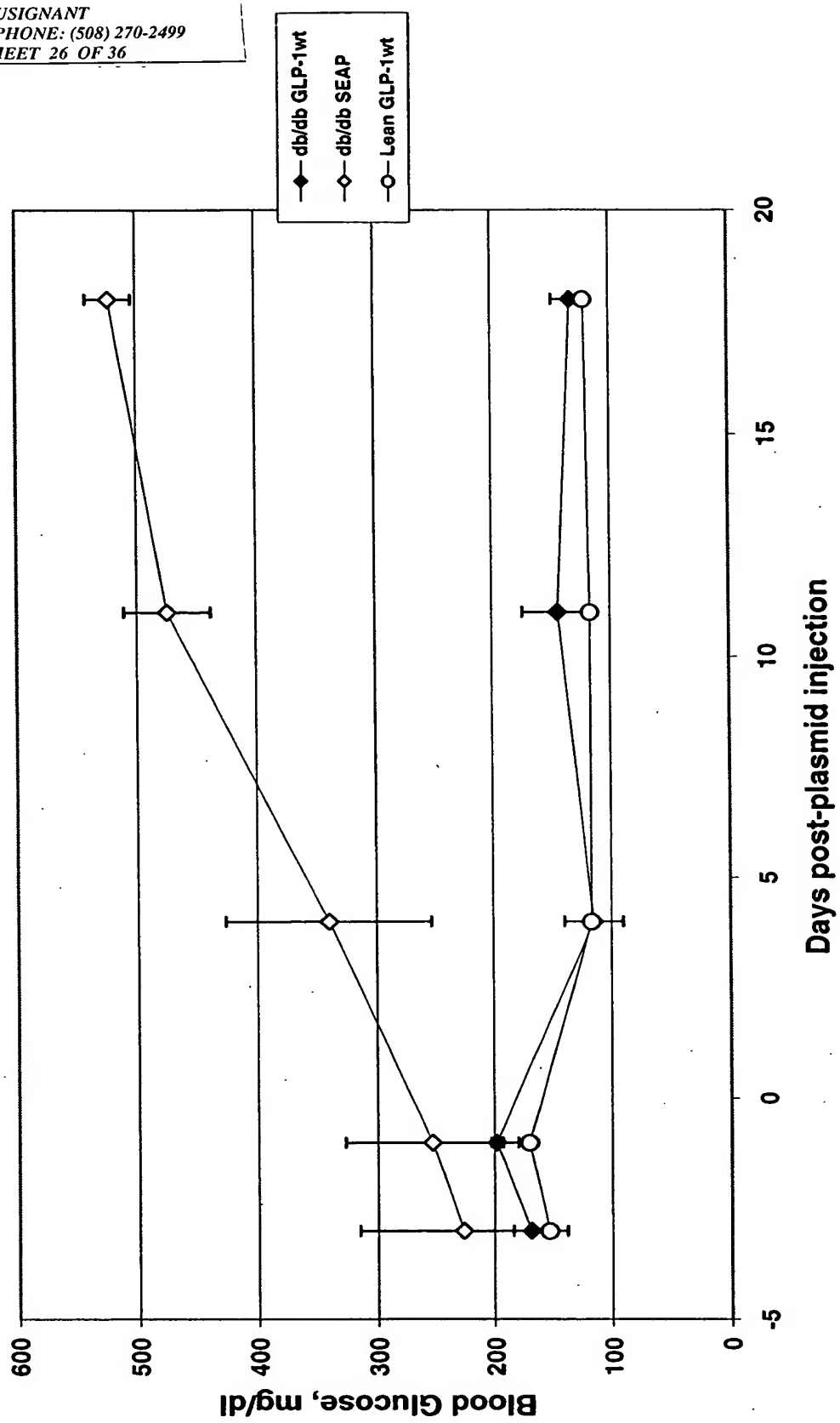

db/db GLP-1wt
db/db SEAP
Lean GLP-1wt
Blood Glucose, mg/dl
600
500
400
300
200
100
0
Days post-plasmid injection
-5
0
5
10
15
20

Figure 26

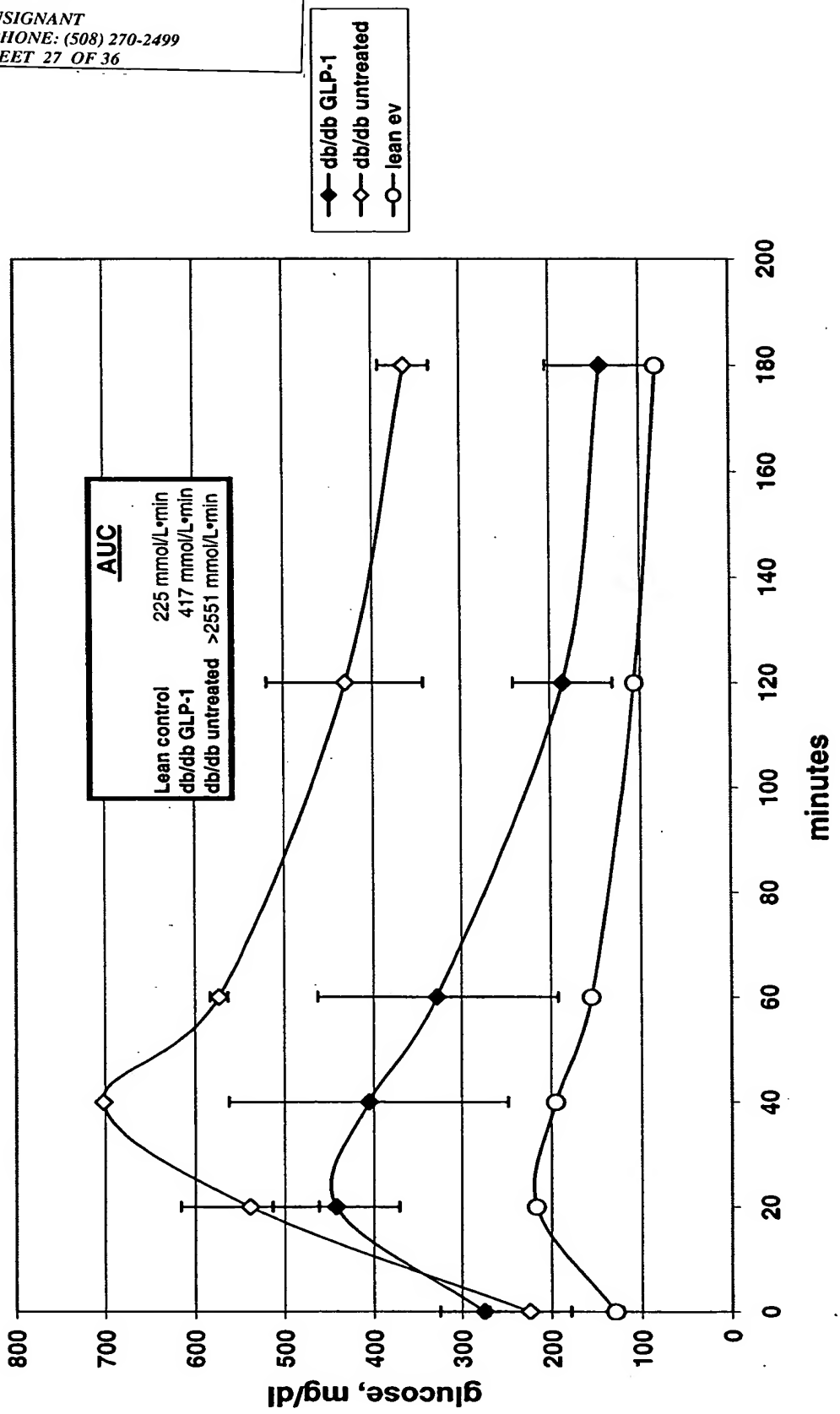
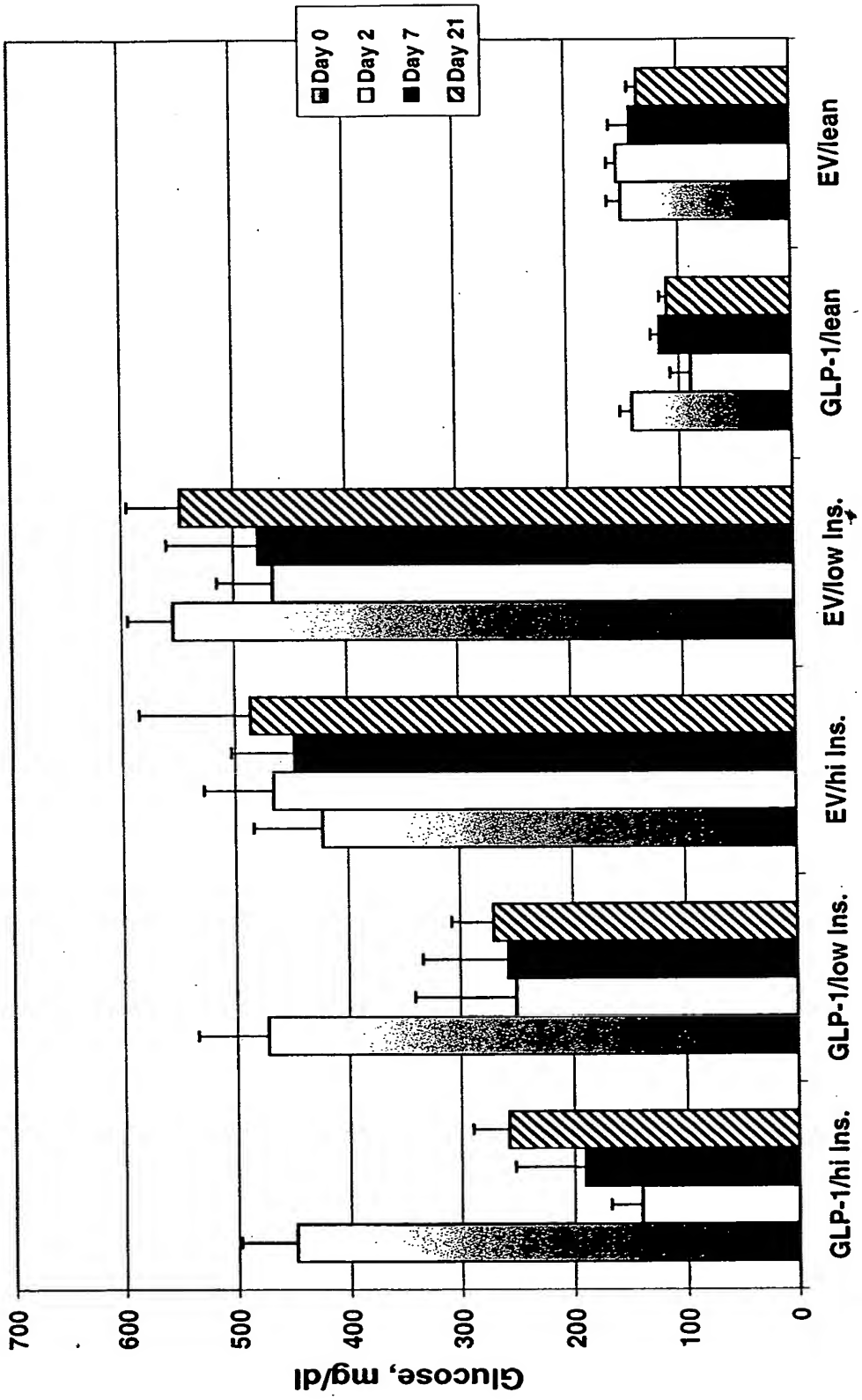

db/db GLP-1
db/db untreated
lean ev
AUC
Lean control 225 mmol/L•min
db/db GLP-1 417 mmol/L•min
db/db untreated >2551 mmol/L•min
glucose, mg/dl
minutes
800
700
600
500
400
300
200
100
0
0
20
40
60
80
100
120
140
160
180
200

Figure 27


Day 0
Day 2
Day 7
Day 21
Glucose, mg/dl
700
600
500
400
300
200
100
0
GLP-1/hi Ins.
GLP-1/low Ins.
EV/hi Ins.
EV/low Ins.
GLP-1/lean
EV/lean

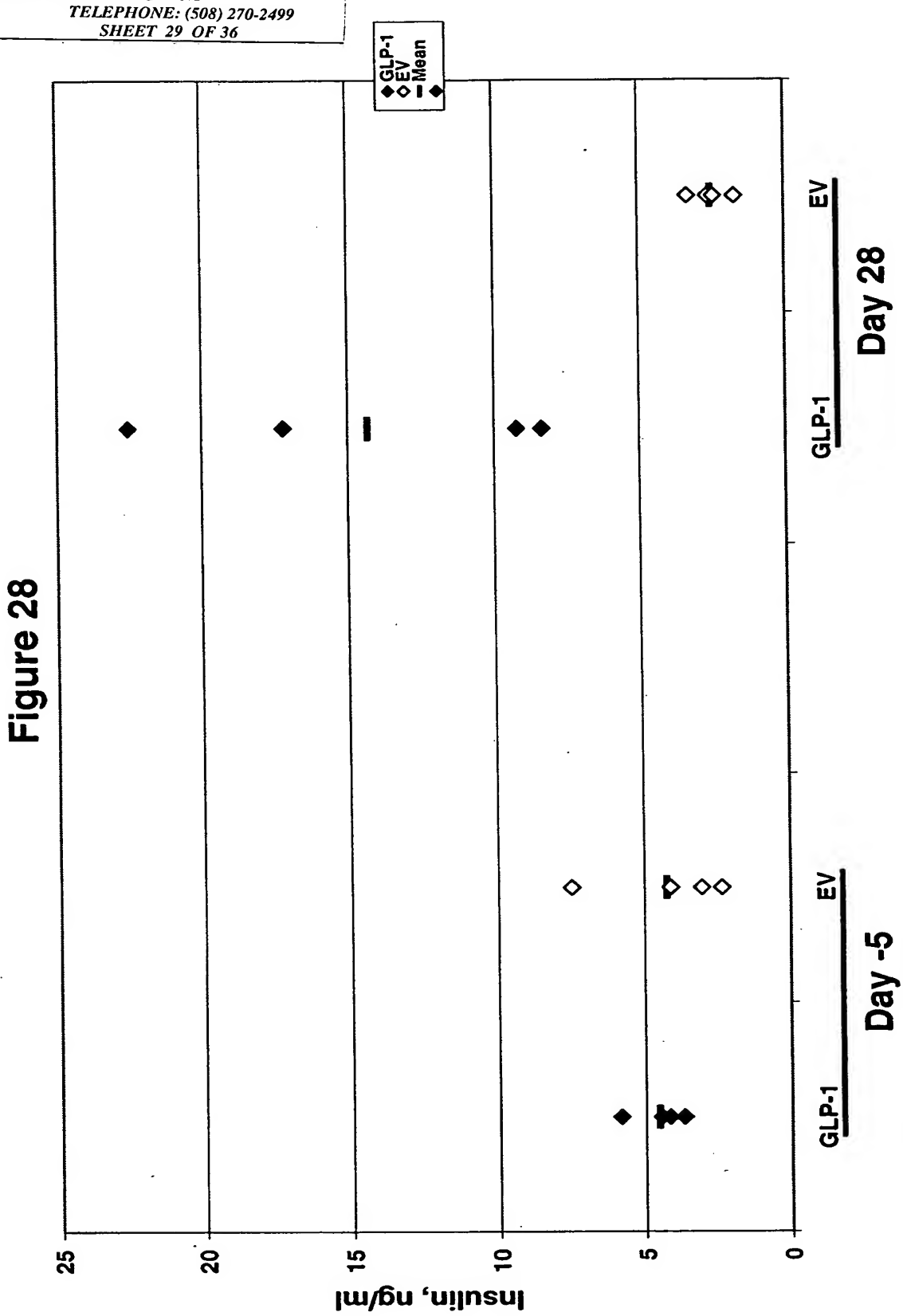

GLP-1
EV
Mean
Insulin, ng/ml
25
20
15
10
5
0
GLP-1
EV
Day -5
GLP-1
EV
Day 28

Figure 28

Figure 29

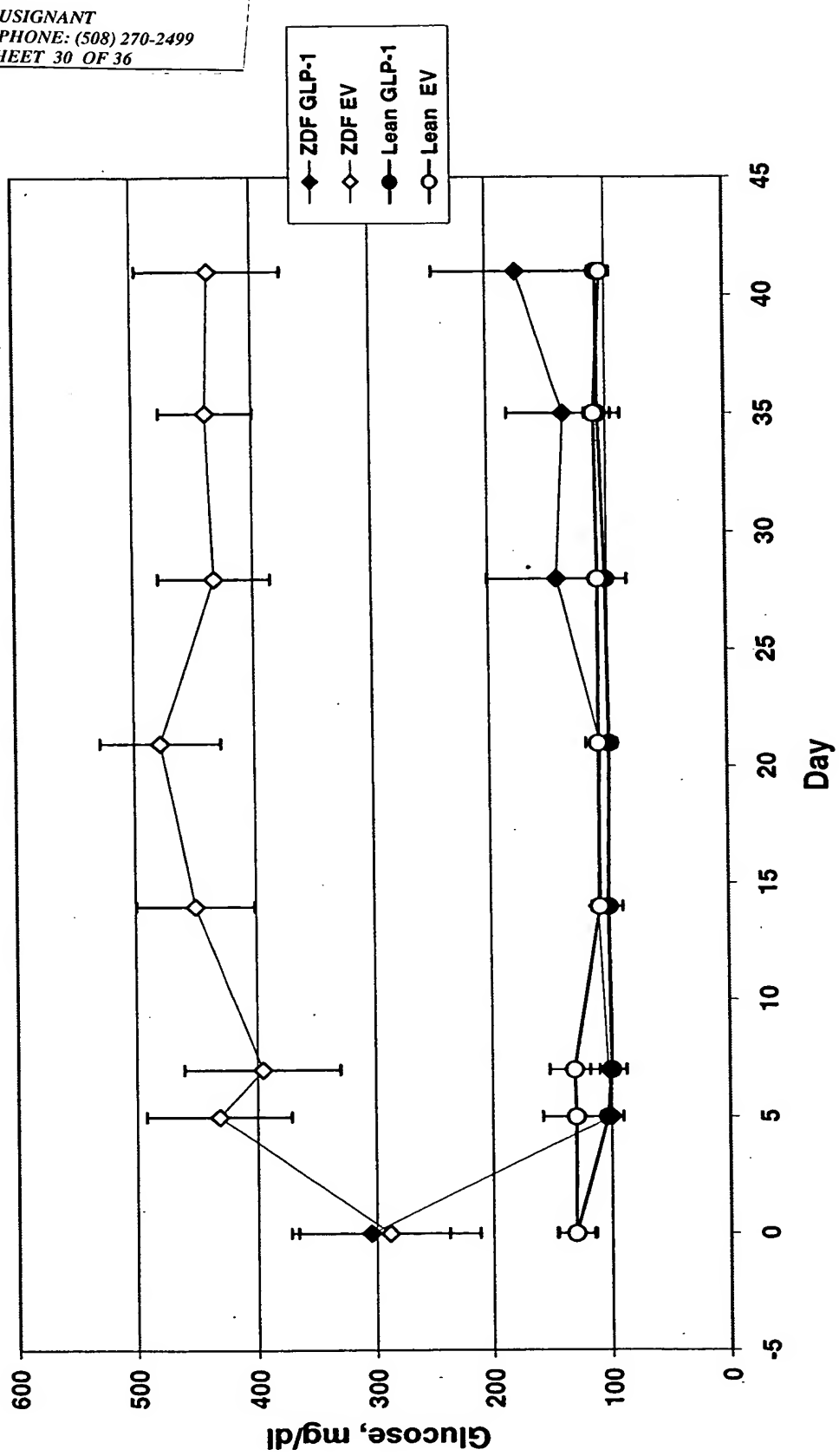

ZDF GLP-1
ZDF EV
Lean GLP-1
Lean EV
Glucose, mg/dl
600
500
400
300
200
100
0
Day
45
40
35
30
25
20
15
10
5
0
-5

Figure 30

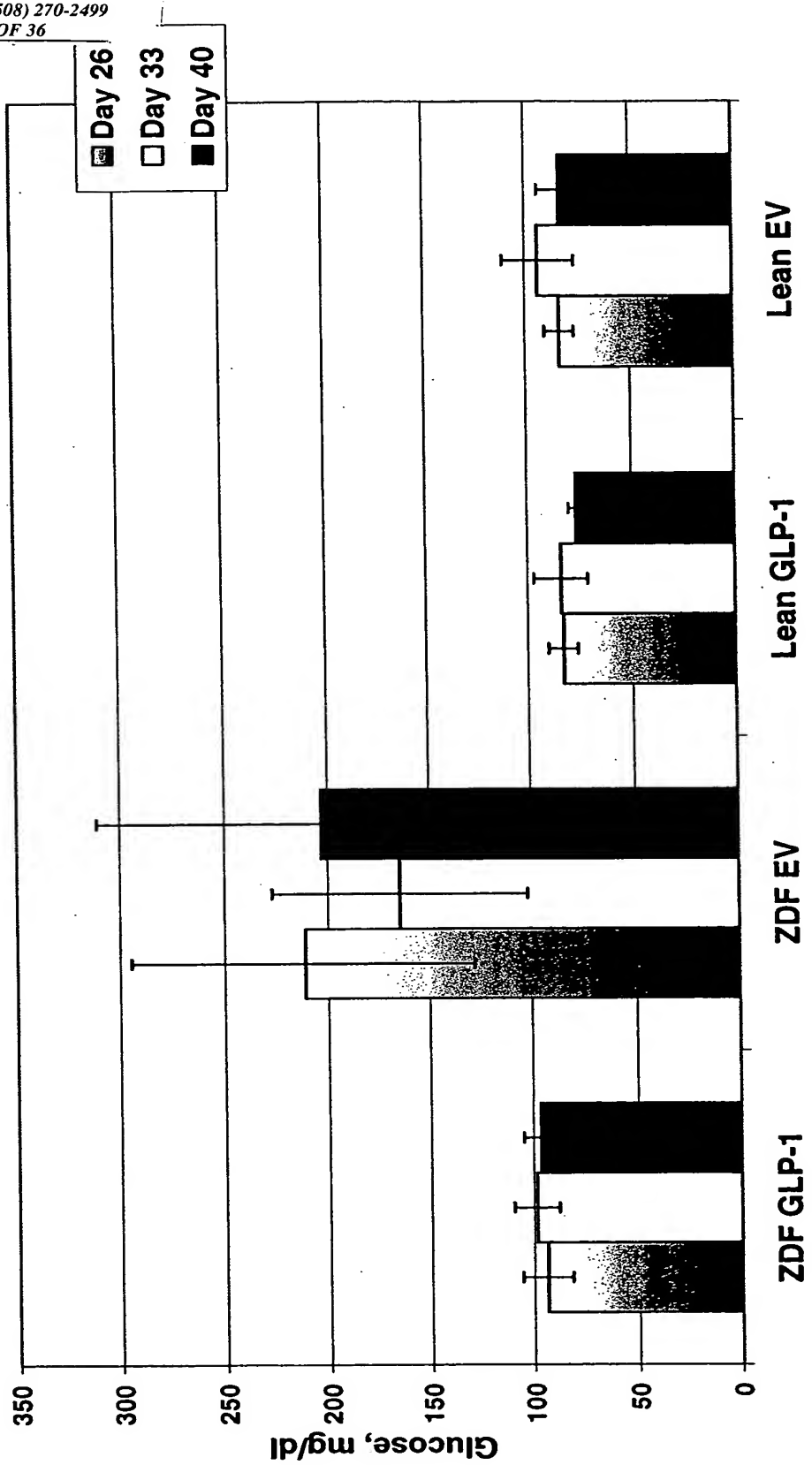

Day 26
Day 33
Day 40
Glucose, mg/dl
350
300
250
200
150
100
50
0
Lean EV
Lean GLP-1
ZDF EV
ZDF GLP-1

Figure 31

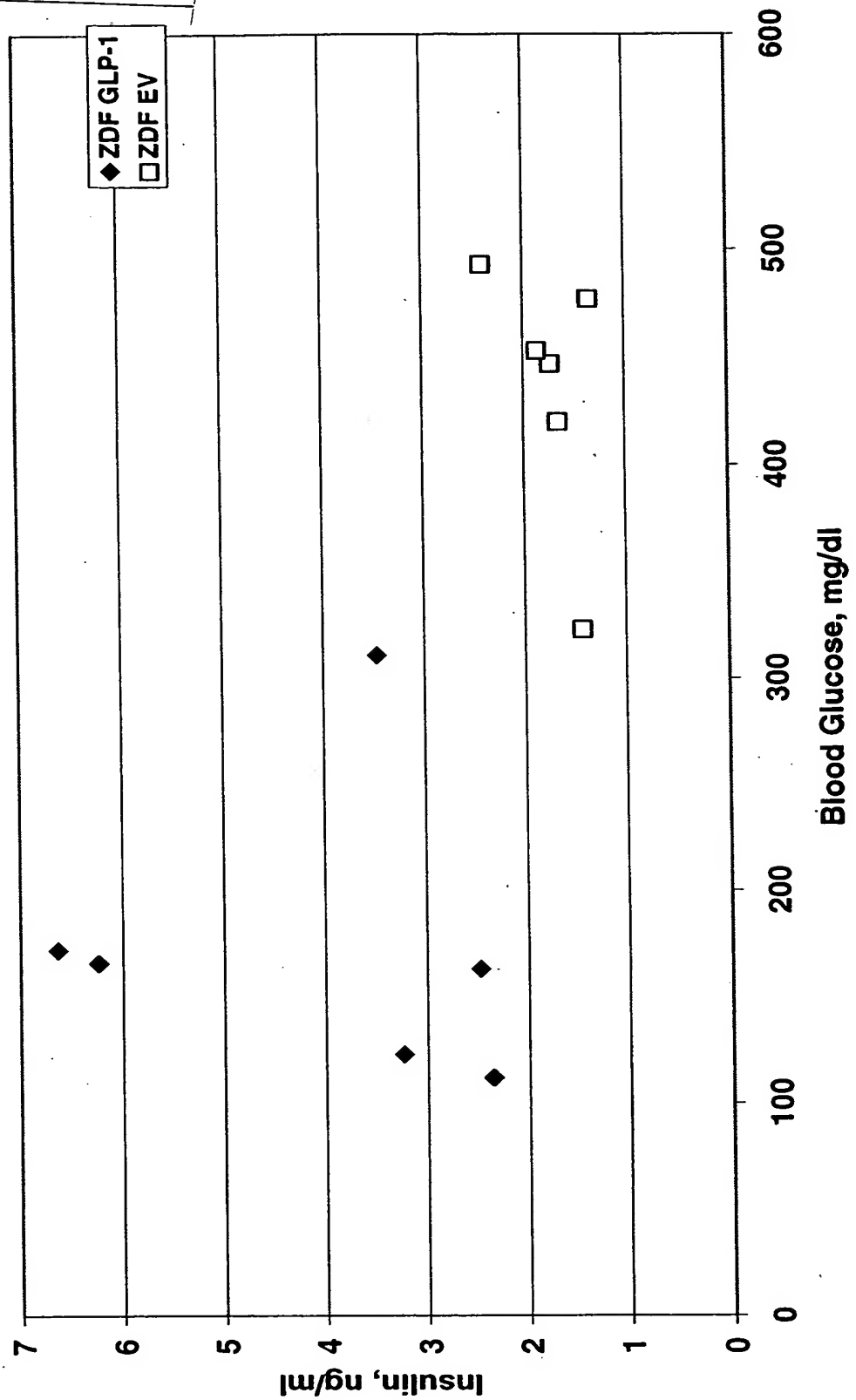

ZDF GLP-1
ZDF EV
Insulin, ng/ml
0
1
2
3
4
5
6
7
Blood Glucose, mg/dl
0
100
200
300
400
500
600

Figure 32

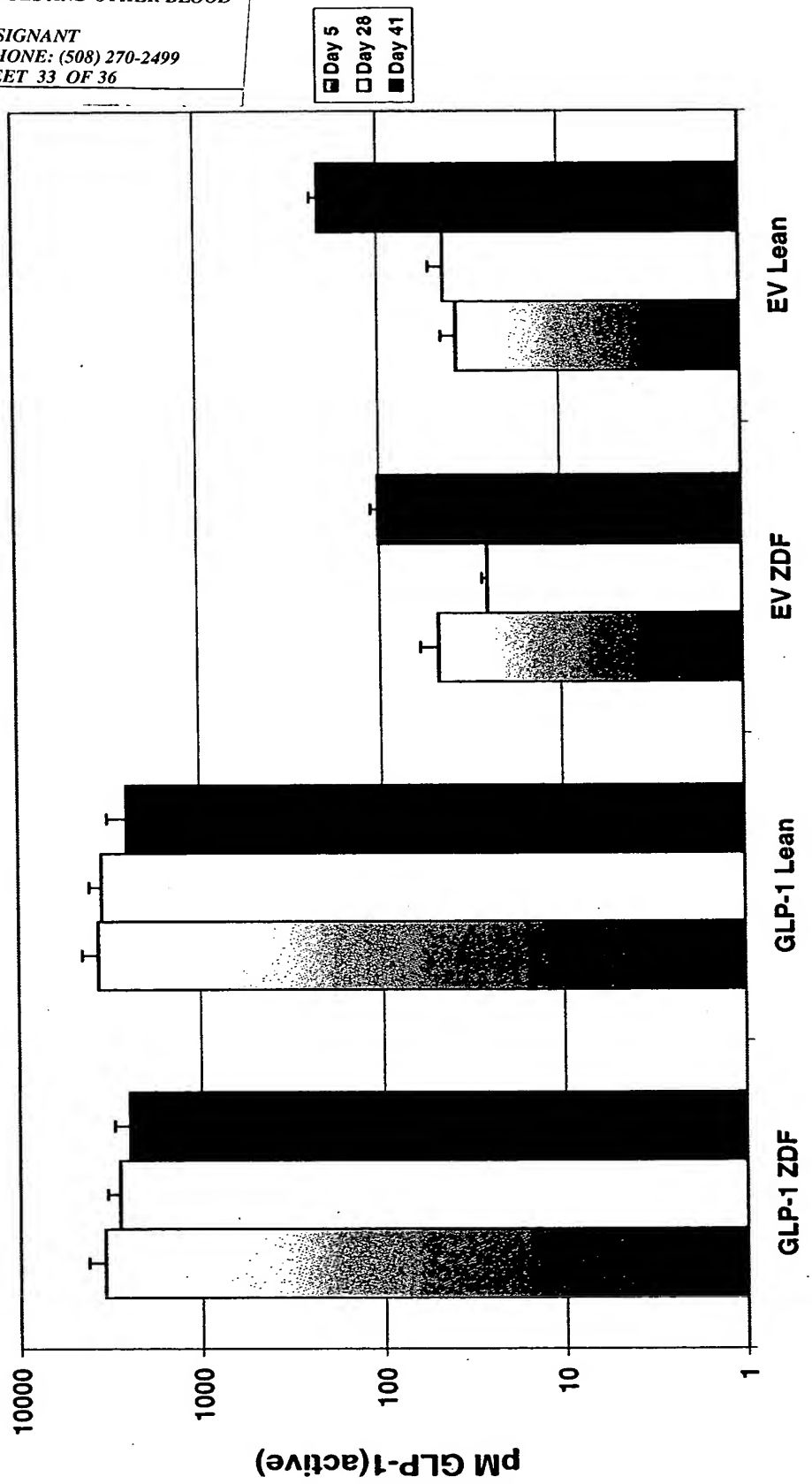

Day 5
Day 28
Day 41
EV Lean
EV ZDF
GLP-1 Lean
GLP-1 ZDF
10000
1000
100
10
1
pM GLP-1(active)

Figure 33

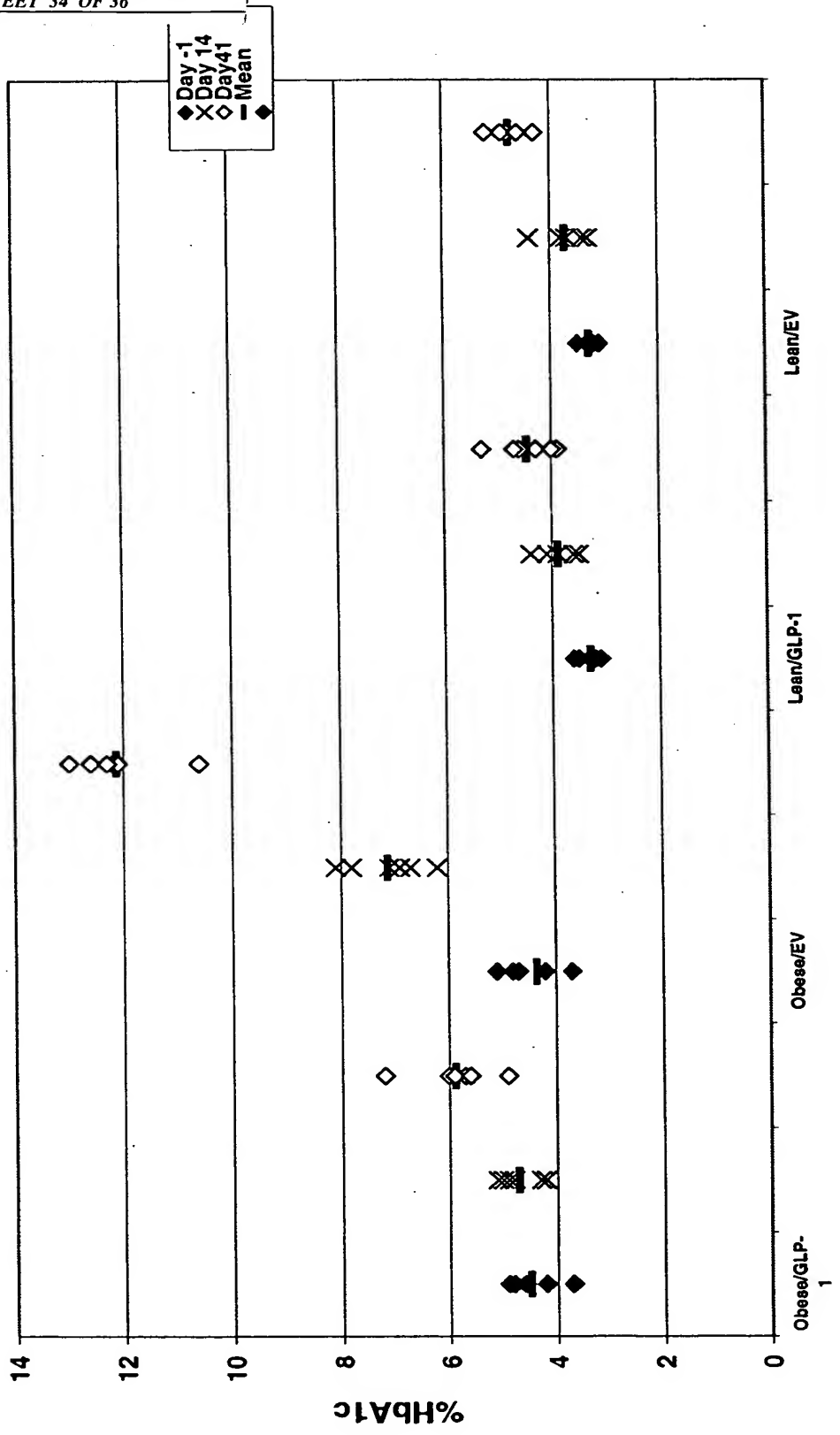

Day -1
Day 14
Day41
Mean
%HbA1c
14
12
10
8
6
4
2
0
Lean/EV
Lean/GLP-1
Obese/EV
Obese/GLP-1

Figure 34

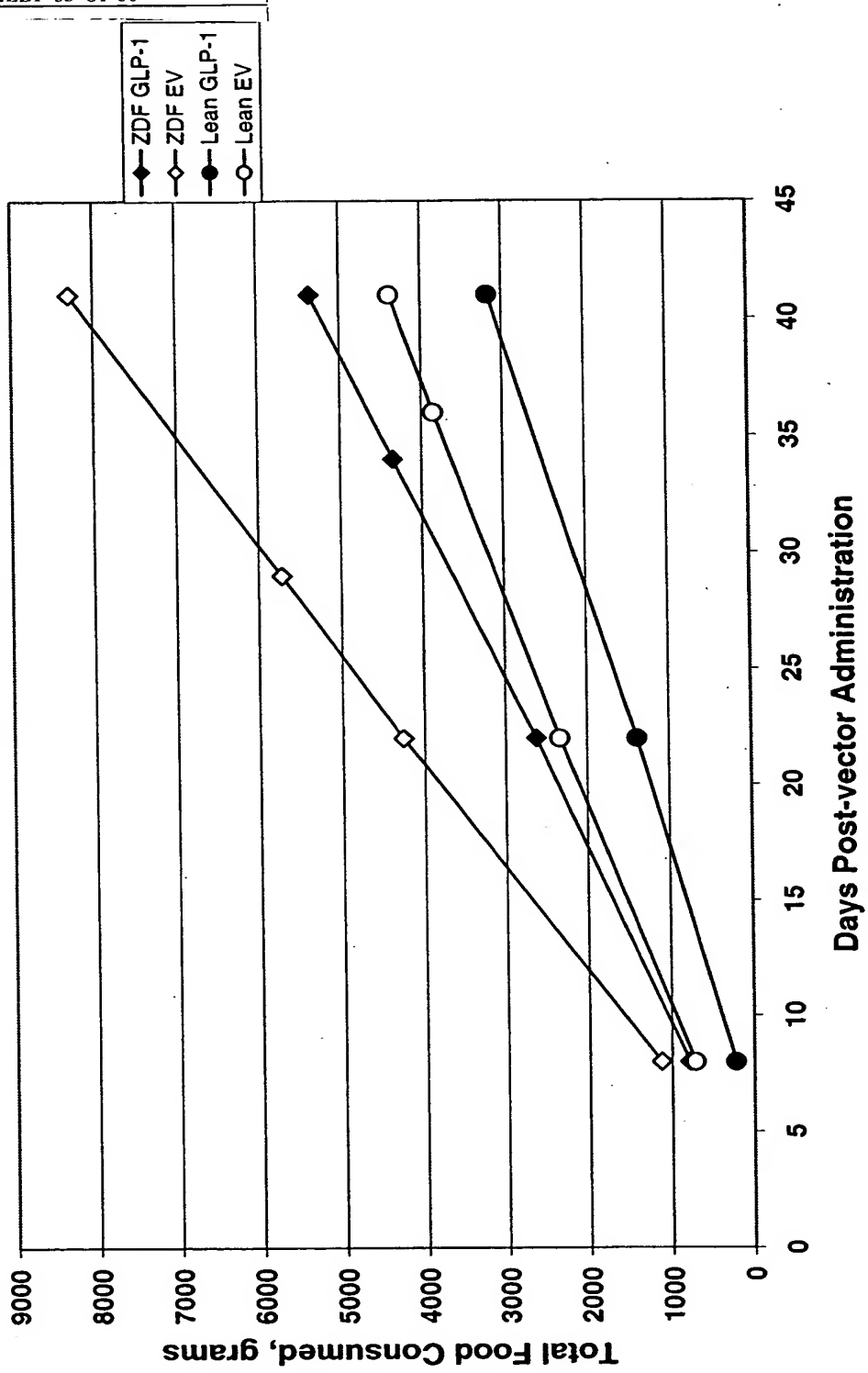
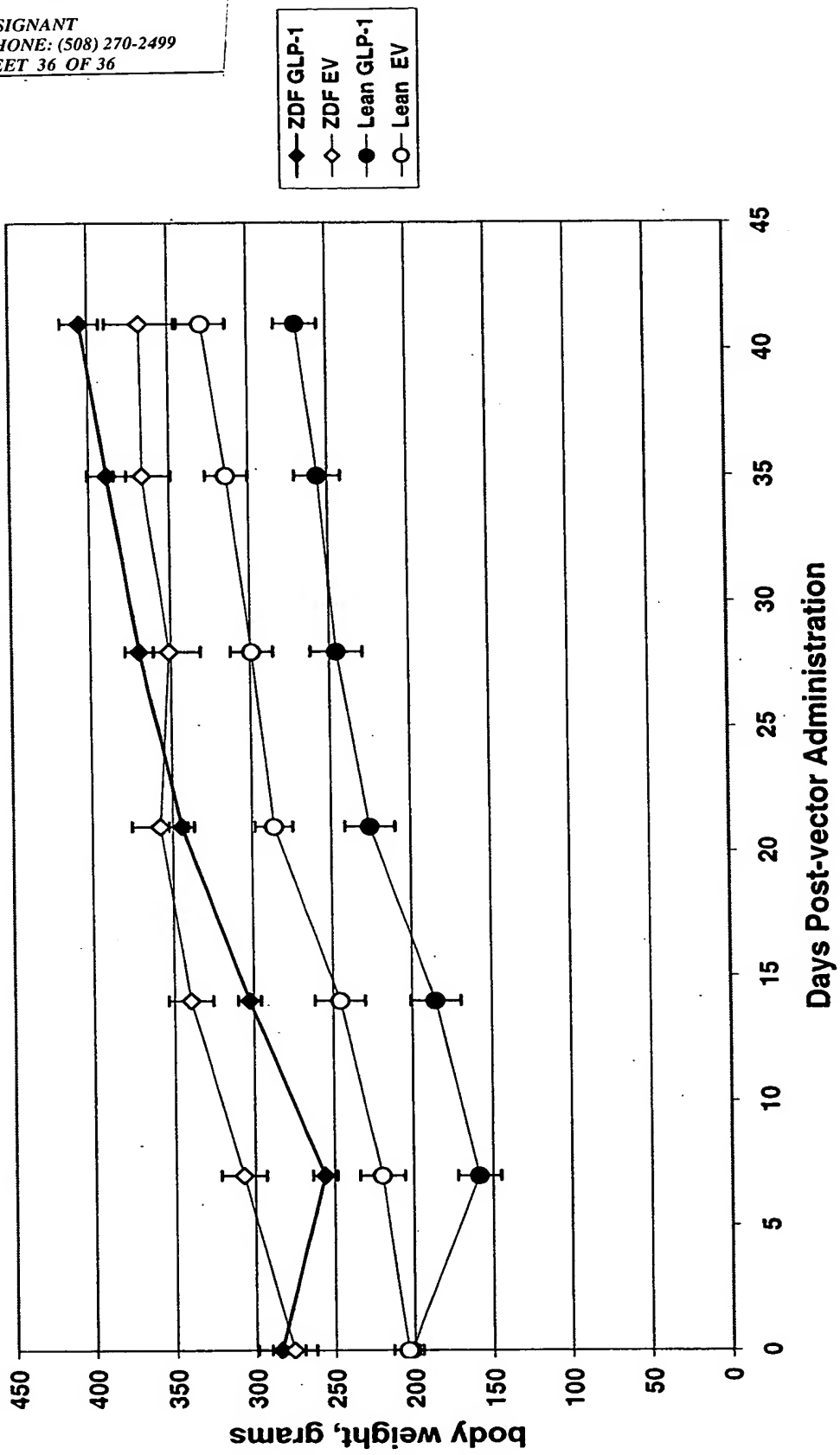

ZDF GLP-1
ZDF EV
Lean GLP-1
Lean EV
Total Food Consumed, grams
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
Days Post-vector Administration
0
5
10
15
20
25
30
35
40
45

Figure 35


ZDF GLP-1
ZDF EV
Lean GLP-1
Lean EV
body weight, grams
450
400
350
300
250
200
150
100
50
0
0
5
10
15
20
25
30
35
40
45
Days Post-vector Administration